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(54) Title: PROCESS FOR THE PRODUCTION OF FINE CHEMICALS

(57) Abstract: The present invention relates to a process for the production of the fine chemical in a microorganism, a plant cell, a plant, a plant tissue or in one or more parts thereof. The invention furthermore relates to nucleic acid molecules, polypeptides, nucleic acid constructs, vectors, antisense molecules, antibodies, host cells, plant tissue, propagation material, harvested material, plants, microorganisms as well as agricultural compositions and their use.

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Process for the production of fine chemicals

[0001.0.0.0] The present invention relates to a process for the production of the fine chemical in a microorgansm, a plant cell, a plant, a plant tissue or in one or more parts thereof. The invention furthermore relates to nucleic acid molecules, polypeptides, nucleic acid constructs, vectors, antisense molecules, antibodies, host cells, plant tissue, propagtion material, harvested material, plants, microorganisms as well as agricultural compositions and to their use.

Certain products and by-products of naturally-occurring metabolic [0.002.0.0.0] processes in cells have utility in a wide array of industries, including, but not limited to, the food, feed, cosmetics, and pharmaceutical industries and agriculture. These 10 molecules, collectively termed 'fine chemicals' include molecules such as vitamins for example vitamin A, D, E, K, B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub>, B<sub>12</sub>, C, pantothenic acid, biotin or folic acid; substances with vitamin-like character for example vitamin F, lipoic acid, ubiquinones, choline, myoinsositiol, vitamin U (S-methylmethionine), flavours for example vanillin, coumarin, isoeugenol, eugenol, (R)-carvone, (S)-carvone, menthol, jasmone or 15 farnesol; nutraceuticals for example phytosterols, flavonoids, anthocyanidins, isoflavons or isoprenoids; detergents; fatty acids such as saturated fatty acids, mono unsaturated fatty acids (singular MUFA, plural MUFAS), poly unsaturated fatty acids (singular PUFA, plural PUFAS), waxes or lipids containing said fatty acids; carbohydrates for example cellulose, starch, dextrin, pectin, xanthangum, carrageenan 20 or alginate; sugars for example monosaccharides such as glucose, fructose, manose, sorbose, ribose, ribulose, xylose, xylulose or galactose, disaccharides such as lactose, sucrose, saccharose, maltose, isomaltose or cellobiose, trisaccharides such as raffinose or maltotriose; carboxylic acids for example citric acid,  $\alpha$ -ketoglutaric acid, ferulic acid, sinapic acid or lactic acid; carotinoids for example  $\alpha$ -carotene,  $\beta$ - carotene, 25 zeaxanthine, lutein, astaxanthine, lycopene, phyotoene or phytofluene, amino acids for example lysine, threonine, methionine, tryptophane, phenylalanine or tyrosine, cofactors for example heme or quinines, enzymes for example lipases, esterases, proteases, amylases, glucosidases etc. and other compounds [as described e.g. in Kuninaka, A. (1996) Nucleotides and related compounds, p. 561-612, in Biotechnology 30 vol. 6, Rehm et al., eds. VCH: Weinheim, in Industial Microbiology and Biotechnology, Demain et al., second edition, ASM Press Washington, D.C. 1999, in Ullmann's Encyclopedia of Industrial Chemistry, vol. A27, Vitamins, p. 443-613 (1996) VCH: Weinheim and Ong, A.S., Niki, E. & Packer, L. (1995) Nutrition, Lipids, Health, and Disease Proceedings of the UNESCO/Confederation of Scientific and Technological 35 Associations in Malaysia, and the Society for Free Radical Research, Asia, held Sept. 1-3, 1994 at Penang, Malaysia, AOCS Press, (1995)), enzymes, and all other chemicals described in Gutcho (1983) Chemicals by Fermentation, Noyes Data Corporation, ISBN: 0818805086 and references contained therein]. Carotinoids are added for example to soft drinks, margarines or to animal feed for example to colour 40 egg yolk or the flesh of fish. In the food industry polycarbohydrates are widely used as thickener. Polyunsaturated fatty acids are added for example to infant formulas to create a higher nutrition value of such formulas. PUFAs have for example a positive influence on the cholesterol level of the blood in humans and therefore are useful in the

protection of heart diseases. Fine chemicals for example PUFAS can be isolated from animal sources such as for example fish or produced with microorganisms through the large-scale culture of microorganisms developed to produce and accumulate or secrete large quantities of one or more desired molecules.

- -5 [0003.0.0.0] In large scale fine chemicals are produced with microorganism in the fermentation industry, which is responsible for the manufacturing of at least five major ingredient categories: antibiotics, organic acids, amino acids, enzymes, vitamins and other related products. There are production facilities in all important areas of the world especially in Europe, the US and Asia. Companies continuously try to optimize the 10 production processes, the organisms and thereby increasing the efficiency but, as in the case of amino acids and organic acids, with already high conversion rates based. on feeded carbon source, the limitations of such work become evident. All fermentation processes depend on the efficient utilization of carbohydrates, supplied mainly in the form of oils, glucose or molasses. It is therefore the availability and pricing of these raw 15 materials that influence the competitiveness of fermentation products versus production for example in plants. Amino acids, organic acids and vitamins are offered at very low prices. For such products the question is whether it is still economical to continue fermentation production in future. And that is frequently a question of comparing the availability and pricing of carbohydrates with the future markets.
- 20 [0004.0.0.0] Particularly useful organisms for the production of fine chemicals are microorganisms such as the algae, fungi, bacteria or plants. Through strain selection, a number of mutant strains of microorganisms have been developed which produce an array of desirable compounds including vitamins, amino acids, PUFAs etc. However, selection of strains improved for the production of a particular molecule is a time-consuming and difficult process.
  - [0005.0.0.0] Alternatively the production of fine chemicals can be most conveniently performed via the large scale production of plants developed to produce for example carotinoids, carbohydrates or PUFAS. For example for the production of carotinoids plants such as marigold are used. Particularly well-suited plants for this purpose are sugar producing plants such as sugar beet or sugar cane or oilseed plants containing high amounts of lipid compounds such as rapeseed, canola, linseed, soybean, sunflower, borage and evening primrose. But also other crop plants containing sugars, oils or lipids and fatty acids are well suited as mentioned in the detailed description of this invention. Through conventional breeding, a number of mutant plants have been developed which produce an array of desirable lipids and fatty acids, cofactors and enzymes. However, selection of new plant cultivars improved for the production of a particular molecule is a time-consuming and difficult process or even impossible if the compound does not naturally occur in the respective plant as for example in the case of C<sub>20</sub> and higher C-carbon chain polyunsaturated fatty acids.
- [0006.0.0.0] Carbohydrates are an important dietary nutrient, which is mostly used to supply energy to the body, as well as, a carbon source for synthesis of other compounds such as fats or proteins. Furthermore mono- and disaccharides are widely used in the food and feed industry as sweetener. Saccharides have varying degrees of

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sweetness on a relative scale. Fructose is the sweetest. For example in the United States 22 million tons of sugar and other sweeteners were consumed in 1999. Said natural sweetener consumption includes the consumption of sugar, com sweeteners such as high fructose corn syrup as main product and others such as honey or maple syrup. All natural sugar based sweeteners have a market shar of around 36 to 40 percent.

[0007.0.0.0] Whether unsaturated or saturated fatty acids are preferred in the food and feed industry depends on the intended purpose; thus, for example, lipids with unsaturated fatty acids, specifically polyunsaturated fatty acids, are preferred in human nutrition since they have a positive effect on the cholesterol level in the blood and thus on the possibility of heart disease. They are used in a variety of dietetic foodstuffs or medicaments. In addition PUFAs are commonly used in food, feed and in the cosmetic industry. Poly unsaturated  $\omega$ -3- and/or  $\omega$ -6-fatty acids are an important part of animal feed and human food. Because of the common composition of human food poly unsaturated  $\omega$ -3-fatty acids, which are an essential component of fish oil, should be added to the food to increase the nutritional value of the food; thus, for example, poly unsaturated fatty acids such as docosahexaenoic acid or eicosapentaenoic acid are added as mentioned above to infant formula to increase its nutritional value.

[0008.0.0.0] Vitamins such as vitamin C, vitamin B12 or vitamin B2 are typically produced with microorganism as mentioned above in the fermentation industry. Vitamin C can be produced generally in a combined process using biotransformation steps in combination with classical chemical synthesis. In another production process vitamin C is produced by fermentation alone. In general organisms such as Arthrobacter, Gluconobacter, Corynebacterium, Brevibacterium or Erwinia are used for vitamin C production. Vitamin B2 and vitamin B12 are produced with organisms such as Bacillus, Streptomyces, Citrobacter, Klebsiella, Propionibacterium or Ashbya in large scale fermentation.

[0009.0.0.0] Commonly vitamin E and A are procuded in a classical chemical process or isolated from as natural vitamin E from plant oils. Vitamin E is an important natural fat-soluble antioxidants. As such, vitamin E protects cell membranes from the damage caused by free radicals. High doses of vitamin E have also been linked to a decreased ability of the blood to clot, which may be beneficial in those individuals at risk for heart disease by reducing the risk of heart attack. A vitamin E deficiency leads to pathophysiological situations in humans and animals. Of the different types of vitamin E, the alpha tocopherol form is typically considered the "gold standard" in terms of antioxidant activity - although the most recent research suggests that the other chemical forms may possess equivalent or superior antioxidant protection. Vitamin E compounds therefore are of high economical value as additives in the food and feed sectors, in pharmaceutical formulations and in cosmetic applications. Vitamin A is another fat-soluble vitamin that is part of a family of compounds including retinol, retinal and beta-carotene. Beta-carotene is also known as pro-vitamin A because it can be converted into vitamin A when additional levels are required. Vitamin A is needed by all of the body's tissues for general growth and repair processes and is especially important for bone formation, healthy skin/hair, night vision and function of the immune

system. Vitamin A may help boost immune system function and resistance to infection. Vitamin A derivatives are widely used in cosmetics and dermatological treatments for skin preparations designed to combat skin aging and treat acne. Vitamin A has been used for decades as a treatment for various vision-related conditions, including night blindness, cataracts, conjunctivitis, retinopathy and macular degeneration.

[0010.0.0.0] An economical method for producing of vitamins such as vitamin C, B2, B12 or vitamin E and food- and feedstuffs with increased vitamin content are therefore very important. Particularly economical methods are biotechnological methods utilizing vitamin-producing organisms, which are either natural or optimized by genetic modification.

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[0011.0.0.0] Carotenoids are a large family of compounds including over 600 members such as  $\beta$ -carotene, lycopene or lutein. Carotenoids are widely distributed in fruits and vegetables and are responsible, along with flavonoids, for contributing the color to many plants (a rule of thumb is the brighter, the better). In terms of nutrition,  $\beta$ -carotene's primary role is as mentioned above a precursor to vitamin A.  $\beta$ -carotene as most other carotenoids, is a powerful antioxidant — so it has been recommended to protect against a variety of diseases such as cancer, cataracts and heart disease.

[0012.0.0.0] The introduction of a new gene or new genes for the synthesis of fine chemicals into an organism or cell may not just increase the biosynthetic flux towards an end product it may also increase or create de novo a new compound composition. Similarly, other genes involved in the import of nutrients necessary for the biosynthesis of one or more fine chemicals (e.g., fatty acids, polar and neutral lipids, vitamins, enzymes etc.) may be increased in number or activity such that these precursors, cofactors, or intermediate compounds are increased in concentration within the cell or within the storing compartment thus increasing further the capability of the cell to produce the fine chemical as described herein.

[0013.0.0.0] Amino acids are used in many branches of industry, including the food, animal feed, cosmetics, pharmaceutical and chemical industries. Amino acids such as D,L-methionine, L-lysine or L-threonine are used in the animal feed industry. The essential amino acids valine, leucine, isoleucine, lysine, threonine, methionine, tyrosine, phenylalanine and tryptophan are particularly important for the nutrition of mammals especially humans and a number of livestock species. Glycine, L-methionine and tryptophan are all used in the pharmaceutical industry. Glutamine, valine, leucine, isoleucine, histidine, arginine, proline, serine and alanine are used in the pharmaceutical and cosmetics industries. Threonine, tryptophan and D,L-methionine are widely used feed additives (Leuchtenberger, W. (1996) Amino acids - technical production and use, pp. 466-502 in Rehm et al., (Ed.) Biotechnology vol. 6, chapter 14a, VCH Weinheim). Moreover, amino acids are suitable for the chemical industry as precursors for the synthesis of synthetic amino acids and proteins, such as N-acetylcysteine, S-carboxymethyl-L-cysteine, (S)-5-hydroxytryptophan and other subtances described in Ullmann's Encyclopedia of Industrial Chemistry, vol. A2, pp. 57-97, VCH Weinheim, 1985. To prefent physiological malnutritions the human body

has a need for essentiall amino acids such as arginine, histidine, isoleucine, leucine, lysine, methionine, tyrosine, phenylalanine, threonine, tryptophan, and valine. Based on their content of amino acids, foods are often classified as complete, partially complete, or incomplete protein sources. In order for a protein to be complete, it must contain all of the essential amino acids. This is the reason that many nutritionists rank non-meat foods as being incomplete. The foods do contain all amino acids, but some may be in lower proportions than are required, and, therefore, should be combined with another food containing higher amounts of these amino acids or should be supplemented with said essential amino acids.

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- [0014.0.0.0] Over one million tonnes of amino acids are currently produced annually; their market value amounts to over 2.5 billion US dollars. They are currently produced by four competing processes: Extraction from protein hydrolysates, for example L-cystine, L-leucine or L-tyrosine, chemical synthesis, for example of D,L-methionine, conversion of chemical precursors in an enzyme or cell reactor, for example L-phenylalanine, and fermentative production by growing, on an industrial scale, bacteria which have been developed to produce and secrete large amounts of the desired molecule in question. An organism, which is particularly suitable for this purpose is Corynebacterium glutamicum, which is used for example for the production of L-lysine or L-glutamic acid. Other amino acids which are produced by fermentation are, for example, L-threonine, L-tryptophan, L-aspartic acid and L-phenylalanine.
  - [0015.0.0.0] The biosynthesis of the natural amino acids in organisms capable of producing them, for example bacteria, has been characterizied thoroughly; for a review of the bacterial amino acid biosynthesis and its regulation, see Umbarger, H.E. (1978) Ann. Rev. Biochem. 47: 533 606].
- [0016.0.0.0] It is known that amino acids are produced by fermentation of strains of 25 coryneform bacteria, in particular Corynebacterium glutamicum. Due to their great importance, the production processes are constantly being improved. Process improvements can relate to measures regarding technical aspects of the fermentation, such as, for example, stirring and oxygen supply, or the nutrient media composition, such as, for example, the sugar concentration during fermentation, or to the work-up to 30 give the product, for example by ion exchange chromatography, or to the intrinsic performance properties of the microorganism itself. Bacteria from other genera such as Escherichia or Bacillus are also used for the production of amino acids. A number of mutant strains, which produce an assortment of desirable compounds from the group of the sulfur-containing fine chemicals have been developed via strain selection. The 35 performance properties of said microorganisms are improved with respect to the production of a particular molecule by applying methods of mutagenesis, selection and mutant selection. Methods for the production of methionine have also been developed. In this manner, strains are obtained which are, for example, resistant to antimetabolites, such as, for example, the methionine analogues α-methylmethionine, 40

ethionine, norleucine, N-acetylnorleucine, S-trifluoromethylhomocysteine, 2-amino-5-heprenoitic acid, selenomethionine, methionine sulfoximine, methoxine, 1-aminocyclopentanecarboxylic acid or which are auxotrophic for metabolites with regulatory importance and which produce sulfur-containing fine chemicals such as, for example, L-methionine. However, such processes developed for the production of methionine have the disadvantage that their yields are too low for being economically exploitable and that they are therefore not yet competitive with regard to chemical synthesis.

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[0017.0.0.0] Zeh (Plant Physiol., Vol. 127, 2001: 792-802) describes increasing the methionine content in potato plants by inhibiting threonine synthase by what is known as antisense technology. This leads to a reduced threonine synthase activity without the threonine content in the plant being reduced. This technology is highly complex; the enzymatic activity must be inhibited in a very differentiated manner since otherwise auxotrophism for the amino acid occurs and the plant will no longer grow.

[0018.0.0.0] US 5,589,616 teaches the production of higher amounts of amino acids 15 in plants by overexpressing a monocot storage protein in dicots. WO 96/38574, WO 97/07665, WO 97/28247, US 4,886,878, US 5,082,993 and US 5,670,635 are following this approach. That means in all the aforementioned intellectual property rights different proteins or polypeptides are expressed in plants. Said proteins or polypeptides should function as amino acid sinks. Other methods for increasing amino acids such as lysine 20 are disclosed in WO 95/15392, WO 96/38574, WO 89/11789 or WO 93/19190. In this cases speziell enzymes in the amino acid biosynthetic pathway such as the diphydrodipicolinic acid synthase are deregulated. This leads to an increase in the production of lysine in the different plants. Another approach to increase the level of amino acids in plants is disclosed in EP-A-0 271 408. EP-A-0 271 408 teaches the 25 mutagenensis of plant and selection afterwards with inhibitors of certain enzymes of amino acid biosynthetic pathway.

[0019.0.0.0] Methods of recombinant DNA technology have also been used for some years to improve Corynebacterium strains producing L-amino acids by amplifying individual amino acid biosynthesis genes and investigating the effect on amino acid production.

[0020.0.0.0] As described above, the essential amino acids are necessary for humans and many mammals, for example for livestock. L-methionine is important as methyl group donor for the biosynthesis of, for example, choline, creatine, adrenaline, bases and RNA and DNA, histidine, and for the transmethylation following the formation of S-adenosylmethionine or as a sulfhydryl group donor for the formation of cysteine. Moreover, L-methionine appears to have a positive effect in depression.

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[0021.0.0.0] Improving the quality of foodstuffs and animal feeds is an important task of the food-and-feed industry. This is necessary since, for example, certain amino acids, which occur in plants are limited with regard to the supply of mammals. Especially advantageous for the quality of foodstuffs and animal feeds is as balanced as possible an amino acid profile since a great excess of an amino acid above a specific concentration in the food has no further positive effect on the utilization of the food since other amino acids suddenly become limiting. A further increase in quality is only possible via addition of further amino acids, which are limiting under these conditions. The targeted addition of the limiting amino acid in the form of synthetic products must be carried out with extreme caution in order to avoid amino acid imbalance. For example, the addition of an essential amino acid stimulates protein digestion, which may cause deficiency situations for the second or third limiting amino acid, in particular. In feeding experiments, for example casein feeding experiments, the additional provision of methionine, which is limiting in casein, has revealed the fatty degeneration of liver, which could only be alleviated after the additional provision of tryptophan.

[0022.0.0.0] To ensure a high quality of foods and animal feeds, it is therefore necessary to add fine chemicals that means a plurality of compounds such as amino acids, vitamins, organic acids, PUFAS etc. in a balanced manner to suit the organism. Such supplemented food is named as "functional foods" or "nutraceuticals". Nutraceuticals shall provide a health benefit to humans beyond basic nutrition. Functional foods have health-promoting or disease-preventing effects. Examples include omega-3 fatty acids (found in many fish, flaxseed oil, soybean oil, canola oil, and walnuts), which reduce risk of coronary heart disease and lycopene in tomatoes, which has been associated with reduced risk of certain cancers.

[0023.0.0.0] From a practical standpoint it would be of great advantage to produce an organism such as a microorganism or a plant containing a combination of different fine chemicals such as amino acids, vitamins, organic acids, carotenoids, PUFAS etc. at the same time in an sufficient amount to provide optimal growth and health benefit to animals or humans instead of combining different food or supplementing food or feed with different fine chemicals.

[0024.0.0.0] It is therefore an object of the present invention to develop an inexpensive process for the synthesis of a combination of fine chemicals such as amino acids like tryptophane, proline, arginine, phenylalanine, tyrosine, alanine, glycine, threonine, serine, valine, isoleucine or leucine especially essential amino acids such as tryptophane, arginine, phenylalanine, tyrosine, threonine, valine, isoleucine or leucine, carbohydrates such as raffinose, maltose or inositol, vitamins such as  $\gamma$ -,  $\alpha$ - or  $\beta$ -tocopherol, organic acids such as ferulic acid, malate or sinapic acid, carotenoids such as  $\beta$ -carotene etc. at the same time in an sufficient amount to provide optimal growth and health benefit to animals or humans

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[0025.0.0.0] It was now found that this object is achieved by providing the process according to the invention described herein and the embodiments characterized in the claims.

[0026.0.0.0] Accordingly, in a first embodiment, the invention relates to a process for the production of a fine chemical, whereby the fine chemical is at least one compound selected from the group consisting of tryptophane, proline, arginine, phenylalanine, tyrosine, alanine, glycine, threonine, serine, valine, isoleucine, leucine, raffinose, maltose, inositol, ferulic acid, malate, γ- tocopherol, α- tocopherol, β-tocopherol, cerotic acid, lignoceric acid, putrescine, sinapic acid, 3,4-dihydroxyphenylaline (= DOPA), stearic acid and β-carotene. Accordingly, in the present invention, the term "the fine chemical" as used herein relates to an amino acid selected from the group consisting of tryptophane, proline, arginine, phenylalanine, tyrosine, alanine, glycine, threonine, serine, valine, isoleucine and leucine; a vitamin selected from the group consisting of γtocopherol, α- tocopherol and β-tocopherol, a fatty acid selected from the group consisting of cerotic acid, lignoceric acid and stearic acid, an organic acid selected from the group consisting of ferulic acid, malate and sinapic acid or a compound selected from the group consisting of raffinose, putrescine, 3,4-dihydroxyphenylaline (= DOPA) and β-carotene or mixtures thereof containing at least two, three, four or five compounds selected from the aforementioned groups, preferably 6, 7, 8 or 9 compounds selected from the aforementioned groups, most preferably 10, 11, 12, 13, 14, 15, 16, 17 or more compounds selected from the aforementioned groups. Further, the term "the fine chemicals" as used herein also relates to fine chemicals comprising at least one compound selected from the group consisting of tryptophane, proline, arginine, phenylalanine, tyrosine, alanine, glycine, threonine, serine, valine, isoleucine, leucine, raffinose, maltose, inositol, ferulic acid, malate, γ- tocopherol, α- tocopherol, βtocopherol, cerotic acid, lignoceric acid, putrescine, sinapic acid, 3,4dihydroxyphenylaline (= DOPA), stearic acid and β-carotene.

[0027.0.0.0] In one embodiment, the term "the fine chemical" or "fine chemical" means at least one compound selected from the group consisting of L-tryptophane, L-proline, L-arginine, L-phenylalanine, L-tyrosine, L-alanine, glycine, L-threonine, L-serine, L-valine, L-isoleucine, L-leucine, raffinose, maltose, inositol, ferulic acid, malate, γ-tocopherol, α- tocopherol, β-tocopherol, cerotic acid, lignoceric acid, putrescine, sinapic acid, 3,4-dihydroxyphenylaline (= DOPA), stearic acid and β-carotene. Throughout the specification the term "the fine chemical" means the aforementioned compounds, its salts, ester or amids in free form or bound to other chemical compounds especially proteins. In a preferred embodiment, the term "the fine chemical" or "fine chemical" means at least one compound selected from the group consisting of L-tryptophane, L-proline, L-arginine, L-phenylalanine, L-tyrosine, L-alanine, glycine, L-threonine, L-serine, L-valine, L-isoleucine and L-leucine in free form or its salts or bound to proteins.

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[0028.0.0.0] Accordingly, the present invention relates to a process for the production of fine chemical comprising

- increasing or generating the biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 5 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 10 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 in a non-human organism, or 15 in one or more parts thereof; and
  - (b) growing the organism under conditions which permit the production of the fine chemical in said organism.
  - [0029.0.0.0] Comprises/comprising and grammatical variations thereof when used in this specification are to be taken to specify the presence of stated features, integers, steps or components or groups thereof, but not to preclude the presence or addition of one or more other features, integers, steps, components or groups thereof.
    - [0030.0.0.0] Preferably, this process further comprises the step of recovering the fine chemical, which is synthesized by the organism from the organism and/or from the culture medium used for the growth or maintainance of the organism. The term "recovering" means the isolation of the fine chemical in different purities, that means on the one hand harvesting of the biological material, which contains the fine chemical without further purification and on the other hand purities of the fine chemical between 5% and 100% purity, preferred purities are in the range of 10% and 99%. In one embodiment, the purities are 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95% or 99% or more.
    - [0031.0.0.0] Advantageously the process for the production of the fine chemical leads to an enhanced production of the fine chemical. The terms "enhanced" or "increase" mean at least a 10%, 20%, 30%, 40% or 50%, preferably at least 60%, 70%, 80%, 90% or 100%, more preferably 150%, 200%, 300%, 400% or 500% higher production of the fine chemical in comparison to the reference as defined below, e.g. that means in comparison to an organism without the aforementioned modification of the activity of a protein having the biological activity represented by a protein as

depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394.

[0032.0.0.0] Surprisingly it was found, that the transgenic expression of the Kluyveromyces lactis, Cryptococcus neoformans, Neurospora crassa, Penicillium marneffei. Mucor rouxii. Schizophyllum commune. Paracoccidioides brasiliensis. Aspergillus fumigatus, Suillus bovinus, Candida albicans, Trichoderma reesei, Ashbya 15 gossypii, Yarrowia lipolytica, Ustilago maydis, Emericella nidulans, Trichomonas vaginalis, Colletotrichum trifolii, Blumeria graminis, Dictyostelium discoideum, Saccaromyces cerevisiae, Schizosaccharomyces pombe, Entamoeba histolytica, Oryza sativa, Brassica napus, Glycine max, Beta vulgaris, Lotus japonicus, Zinnia elegans, Zea mays, Cicer arietinum, Arabidopsis thaliana, Hordeum vulgare, Nicotiana 20 tabacum, Gossypium hirsutum, Physcomitrella patens, Fucus distichus, Medicago truncutula, Homo sapiens, Caenorhabditits elegans, Tigriopus japonicus, Rhopalosiphum padi, Mus musculus, Discopyge ommata, Canis lupus, Drosophila melanogaster, Anopheles gambiae, Aplysia california, Ciona savignyi, Ciona intestinalis, Hemicentrotus pulcherrimus, Giardia lamblia, Gallus gallus, Brachydanio 25 rerio, Xenopus laevis, Xenopus tropicalis, Schistosoma japonicum, Schistosoma mansoni, Encephalitozoon cuniculi, Wuchereria bancrofti, Cavia porcellus, Sus scrofa, Rattus norvegicus, Pneumocystis carinii or Pagrus major proteins as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 30 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 35 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 for example in Arabidopsis thaliana conferred an increase in the fine chemical content of the 40

transformed plants.

[0033.0.0.0] In accordance with the invention, the term "organism" as understood herein relates always to a non-human organism, in particular to an animal or plant organism or to a microorganism. Further, the term "animal" as understood herein relates always to a non-human animal.

- [0034.0.0.0] The sequence depicted in SEQ ID NO: 1 (YNL090W) from Saccharomyces cerevisiae has been published in Madaule et al. [1987, "Characterization of two members of the rho gene family from the yeast Saccharomyces cerevisiae"; Proc. Natl. Acad. Sci., USA 84(3):779-83], and named as rho2. The gene encodes as all the other sequences mentioned above and use in the inventive process a non-essential GTPase of the rho/rac subfamily of the ras-like 10 GTPases. The protein may play a role in the establishment of cell polarity or in microtubule assembly. Accordingly, in one embodiment, the process of the present invention comprises the use of a gene product "involved in in the establishment of cell polarity or in microtubule assembly" from Saccaromyces cerevisiae or its homolog, e.g. as shown herein, for the production of the fine chemical, meaning of preferably for the 15 production of essential amino acids, in particular for increasing the amount of an essential amino acid in free or bound form in an organism or a part thereof, as mentioned herein. That means the increase of its biological activity by overexpression of the responsible gene leads to an increase of the fine chemical.
- [0035.0.0.0] The term "biological activity" means the biological function of the protein 20 of the invention. In contrast to the term "biological activity" the term "activity" means the increase in the production of the compound produced by the inventive process. The term "biological activity" preferably refers to for example the enzymatic function, transporter or carrier function, DNA-packaging function, heat shock protein function, recombination protein function or regulatory function of a peptide or protein in an 25 organism, a tissue, a cell or a cell compartment. Suitable substrates are low-molecularweight compounds and also the protein interaction partners of a protein. The term "increase" of the biological function refers, for example, to the increase in binding capacity or binding strength of a protein for at least one substrate in an organism, a tissue, a cell or a cell compartment - for example by one of the methods described 30 herein below - in comparison with the wild type of the same genus and species to which this method has not been applied, under otherwise identical conditions (such as, for example, culture conditions, age of the plants and the like). Increase is also understood as meaning the modification of the substrate specificity as can be expressed for example, by the kcat/Km value. In this context, an increase of the 35 function of at least 10%, advantageously of at least 20%, preferably at least 30%, especially preferably of at least 40%, 50%, 60 %, 70%, 80%, 90% or more, very especially preferably of at least 150%, 200%, 250%, 300% or more, in comparison with the untreated organism is advantageous.

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[0036.0.0.0] Homologues ( = homologs) of the present gene products can be derived from any organisms as long as the homologue confers the herein mentioned activity, in particular, confers an increase in the fine chemical amount or content. Further, in the present invention, the term "homologue" relates to the sequence of an organism having the highest sequence homology to the herein mentioned or listed sequences of all expressed sequences of said organism. However, the person skilled in the art knows, that preferably, the homologue has said the fine chemical increasing activity and, if known, the same biological function or activity in the organism as the YNL090W protein as depicted in SEQ ID NO: 2. In one embodiment, the homolog of the SEQ ID NO: 2 is a homolog having said biological acitivity and being derived from Eukaryot such as plants like the families Anacardiaceae, Asteraceae, Apiaceae, Betulaceae, Boraginaceae, Brassicaceae, Bromeliaceae, Caricaceae, Cannabaceae, Convolvulaceae, Chenopodiaceae, Cucurbitaceae, Elaeagnaceae, Ericaceae, Euphorbiaceae, Fabaceae, Geraniaceae, Gramineae, Juglandaceae, Lauraceae, Leguminosae or Linaceae; algae, fungi or mosses. In another embodiment, the homolog of SEQ ID NO: 2 is a homolog having said acitivity and being derived from bacteria. In a further embodiment, the homolog of the SEQ ID NO: 2 is a homolog having said acitivity and being derived from fungi. I

[0037.0.0.0] Further homologs of are described herein below.

In accordance with the invention, a protein or polypeptide has the "the 20 [0.038.0.0.0] biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 25 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 30 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394" if its de novo activity, or its increased expression directly or indirectly leads to an increased the fine chemical level in the organism or a part thereof, preferably in a cell of said organism and the protein has the above mentioned activities of a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 40 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248,

250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394. During the specification the activity or preferably the 5 biological activity of such a protein or polypeptide or an nucleic acid molecule or sequence encoding such protein or polypeptide is identical or similar if it still has the biological or enzymatic activity of a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 10 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224; 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 15 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394, if it has at least 10% of the original biological or enzymatic activity, preferably 20%, particularly preferably 30%, most particularly 20 preferably 40% in comparison to a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 25 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 30 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 of Kluyveromyces lactis, Cryptococcus neoformans, Neurospora crassa, Penicillium marneffei, Mucor rouxii, Schizophyllum commune, Paracoccidioides brasiliensis, Aspergillus fumigatus, Suillus bovinus, Candida albicans, Trichoderma reesei, Ashbya gossypii, Yarrowia lipolytica, Ustilago 35 maydis, Emericella nidulans, Trichomonas vaginalis, Colletotrichum trifolii, Blumeria graminis, Dictyostelium discoideum, Saccaromyces cerevisiae, Schizosaccharomyces pombe, Entamoeba histolytica, Oryza sativa, Brassica napus, Glycine max, Beta vulgaris, Lotus japonicus, Zinnia elegans, Zea mays, Cicer arietinum, Arabidopsis thaliana, Hordeum vulgare, Nicotiana tabacum, Gossypium hirsutum, Physcomitrella 40 patens, Fucus distichus, Medicago truncutula, Homo sapiens, Caenorhabditits elegans, Tigriopus japonicus, Rhopalosiphum padi, Mus musculus, Discopyge ommata, Canis

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lupus, Drosophila melanogaster, Anopheles gambiae, Aplysia california, Ciona savignyi, Ciona intestinalis, Hemicentrotus pulcherrimus, Giardia lamblia, Gallus gallus, Brachydanio rerio, Xenopus laevis, Xenopus tropicalis, Schistosoma japonicum, Schistosoma mansoni, Encephalitozoon cuniculi, Wuchereria bancrofti, Cavia porcellus, Sus scrofa and/or Pagrus major.

[0039.0.0.0] The terms "increased", "rised", "extended", "enhanced", "improved" or "amplified" relate to a corresponding change of a property in an organism, a part of an organism such as a tissue, seed, root, leave, flower etc. or in a cell and are interchangeable. Preferrably, the overall activity in the volume is increased or enhanced in cases if the increase or enhancement is related to the increase or enhancement of an activity of a gene product, independent whether the amount of gene product or the specific activity of the gene product or both is increased or enhanced or whether the amount, stability or translation efficacy of the nucleic acid sequence or gene encoding for the gene product is increased or enhanced. The terms "reduction", "decrease" or "deletion" relate to a corresponding change of a property in an organism, a part of an organism such as a tissue, seed, root, leave, flower etc. or in a cell. Preferrably, the overall activity in the volume is reduced, decreased or deleted in cases if the reduction, decrease or deletion is related to the reduction, decrease or deletion of an activity of a gene product, independent whether the amount of gene product or the specific activity of the gene product or both is reduced, decreased or deleted or whether the amount, stability or translation efficacy of the nucleic acid sequence or gene encoding for the gene product is reduced, decreased or deleted.

[0040.0.0.0] The terms "increase" or "decrease" relate to a corresponding change of a property an organism or in a part of an organism, such as a tissue, seed, root, leave, flower etc. or in a cell. Preferrably, the overall activity in the volume is increased in cases the increase relates to the increase of an activity of a gene product, independent whether the amount of gene product or the specific activity of the gene product or both is increased or generated or whether the amount, stability or translation efficacy of the nucleic acid sequence or gene encoding for the gene product is increased.

[0041.0.0.0] Under "change of a property" it is understood that the activity, expression level or amount of a gene product or the metabolite content is changed in a specific volume relative to a corresponding volume of a control, reference or wild type, including the de novo creation of the activity or expression.

[0042.0.0.0] The terms "increase" or "decrease" include the change of said property in only parts of the subject of the present invention, for example, the modification can be found in compartment of a cell, like a organelle, or in a part of a plant, like tissue, seed, root, leave, flower etc. but is not detectable if the overall subject, i.e. complete cell or plant, is tested. Preferably, the increase or decrease is found cellular, thus the term "increase of an acitivity" or "increase of a metabolite content" relates to the cellular

increase compared to the wild typ cell. Typically said increase is based on the higher content of the transcribed nucleic acid or the protein translated from said nucleic acid sequence in the modified cell in comparison to the wild type cell.

[0043.0.0.0] Accordingly, the term "increase" or "decrease" means that the specific activity of an enzyme as well as the amount of a compound or metabolite, e.g. of a polypeptide, a nucleic acid molelcule or of the fine chemical of the invention or an encoding mRNA or DNA, can be increased or decreased in a volume.

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[0044.0.0.0] The terms "wild type", "control" or "reference" are exchangeable and can be a cell or a part of organisms such as an organelle or a tissue, or an organism, in particular a microorganism or a plant, which was not modified or treated according to the herein described process according to the invention. Accordingly, the cell or a part of organisms such as an organelle or a tissue, or an organism, in particular a microorganism or a plant used as wild typ, control or reference corresponds to the cell, organism or part thereof as much as possible and is in any other property but in the result of the process of the invention as identical to the subject matter of the invention as possible. Thus, the wild type, control or reference is treated identically or as identical as possible, saying that only conditions or properties might be different which do not influence the quality of the tested property.

[0045.0.0.0] Preferably, any comparison is carried out under analogous conditions. The term "analogous conditions" means that all conditions such as, for example, culture or growing conditions, assay conditions (such as buffer composition, temperature, substrates, pathogen strain, concentrations and the like) are kept identical between the experiments to be compared.

[0046.0.0.0] The "reference", "control", or "wild type" is preferably a subject, e.g. an organelle, a cell, a tissue, an organism, in particular a plant or a microorganism, which was not modified or treated according to the herein described process of the invention and is in any other property as similar to the subject matter of the invention as possible. The reference, control or wild type is in its genome, transcriptome, proteome or metabolome as similar as possible to the subject of the present invention. Preferably, the term "reference-" "control-" or "wild type-"-organelle, -cell, -tissue or --organism, in particular plant or microorganism, relates to an organelle, cell, tissue or organism, in particular plant or micororganism, which is nearly genetically identical to the organelle, cell, tissue or organism, in particular microorganism or plant, of the present invention or a part thereof preferably 95%, more peferred are 98%, even more preferred are 99,00%, in particular 99,10%, 99,30%, 99,50%, 99,70%, 99,90%, 99,99%, 99, 999% or more.. Most preferable the "reference", "control", or "wild type" is a subject, e.g. an organelle, a cell, a tissue, an organism, which is genetically identical to the organism, cell or organelle used according to the process of the invention except that the responsible or acvitivity conferring nucleic acid molecules or the gene product encoded

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by them are amended, manipulated, exchanged or introduced according to the inventive process.

Preferably, the reference, control or wild type differs form the subject of the present invention only in the cellular activity of the polypeptide of the invention, e.g. as result of an increase in the level of the nucleic acid molecule of the present invention or an increase of the specific activity of the polypeptide of the invention, e.g. by or in the expression level or activity of an protein having the biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 15 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or its homologs, its biochemical or genetical causes and the increased amount of 20 the fine chemical.

[0048.0.0.0] In case, a control, reference or wild type differing from the subject of the present invention only by not being subject of the process of the invention can not be provided, a control, reference or wild type can be an organism in which the cause for the modulation of an activity conferring the increase of the fine chemical or expression of the nucleic acid molecule of the invention as described herein has been switched back or off, e.g. by knocking out the expression of responsible gene product, e.g. by antisense inhibition, by inactivation of an activator or agonist, by activation of an inhibitor or antagonist, by inhibition through adding inhibitory antibodies, by adding active compounds as e.g. hormones, by introducing negative dominant mutants, etc. A gene production can for example be knocked out by introducing inactivating point mutations, which lead to an enzymatic activity inhibition or a destabilization or an inhibition of the ability to bind to cofactors etc.

[0049.0.0.0] Accordingly, preferred reference subject is the starting subject of the present process of the invention. Preferably, the reference and the subject matter of the invention are compared after standardization and normalization, e.g. to the amount of total RNA, DNA, or protein or activity or expression of reference genes, like housekeeping genes, such as ubiquitin, actin or ribosomal proteins.

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[0050.0.0.0] A series of mechanisms exists via which a modification of the a protein, e.g. the polypeptide of the invention can directly or indirectly affect the yield, production and/or production efficiency of the amino acid.

[0051.0.0.0] For example, the molecule number or the specific activity of the polypeptide or the nucleic acid molecule may be increased. Larger amounts of the fine chemical can be produced if the polypeptide or the nucleic acid of the invention is expressed *de novo* in an organism lacking the activity of said protein. However, it is also possible to increase the expression of the gene which is naturally present in the organisms, for example by modifying the regulation of the gene, or by increasing the stability of the corresponding mRNA or of the corresponding gene product encoded by the nucleic acid molecule of the invention, or by introducing homologous genes from other organisms which are differently regulated, eg. not feedback sensitive or not feedback regulated.

**[0052.0.0.0]** This also applies analogously to the combined increased expression of the nucleic acid molecule of the present invention or its gene product with that of further enzymes of the biochemical pathway of the fine chemical e.g. of the amino acid biosynthesis pathway, e.g. which are useful for the synthesis of the fine chemicals.

[0053.0.0.0] The increase, decrease or modulation according to this invention can be constitutive, e.g. due to a stable permanent transgenic expression or to a stable mutation in the corresponding endogenous gene encoding the nucleic acid molecule of the invention or to a modulation of the expression or of the behaviour of a gene conferring the expression of the polypeptide of the invention, or transient, e.g. due to an transient transformation or temporary addition of a modulator such as a agonist or antagonist or inducible, e.g. after transformation with a inducible construct carrying the nucleic acid molecule of the invention under control of a induceable promoter and adding the inducer, e.g. tetracycline or as described herein below.

[0054.0.0.0] The increase in activity of the polypeptide amounts in a cell, a tissue, a organelle, an organ or an organism or a part thereof preferably to at least 5%, preferably to at least 20% or at to least 50%, especially preferably to at least 70%, 80%, 90% or more, very especially preferably are to at least 200%, 300% or 400%, most preferably are to at least 500%, 600% or more in comparison to the control, reference or wild type.

[0055.0.0.0] The specific activity of a polypeptide encoded by a nucleic acid molecule of the present invention or of the polypeptide of the present invention can be tested as described in the examples. In particular, the expression of a protein in question in a cell, e.g. a plant cell or a microorganism and the detection of an increase the fine chemical level in comparison to a control is an easy test and can be performed as described in the state of the art.

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[0056.0.0.0] The term "increase" includes, that a compound or an activity is introduced into a cell *de novo* or that the compound or the activity has not been detectable before, in other words it is "generated".

[0057.0.0.0] Accordingly, in the following, the term "increasing" also comprises the term "generating" or "stimulating". The increased activity manifests itself in an increase of the fine chemical.

[0058.0.0.0] In case the biological activity of the Saccaromyces cerevisiae protein YNL090W as depicted in SEQ ID NO: 2, or the biological activity of the of Kluyveromyces lactis, Cryptococcus neoformans, Neurospora crassa, Penicillium marneffei, Mucor rouxii, Schizophyllum commune, Paracoccidioides brasiliensis, Aspergillus fumigatus, Suillus bovinus, Candida albicans, Trichoderma reesei, Ashbya gossypii, Yarrowia lipolytica, Ustilago maydis, Emericella nidulans, Trichomonas vaginalis, Colletotrichum trifolii, Blumeria graminis, Dictyostelium discoideum, Schizosaccharomyces pombe, Entamoeba histolytica, Oryza sativa, Brassica napus, Glycine max. Beta vulgaris, Lotus japonicus, Zinnia elegans, Zea mays, Cicer 15 arietinum, Arabidopsis thaliana, Hordeum vulgare, Nicotiana tabacum, Gossypium hirsutum, Physcomitrella patens, Fucus distichus, Medicago truncutula, Homo sapiens, Caenorhabditits elegans. Tigriopus japonicus, Rhopalosiphum padi, Mus musculus, Discopyge ommata, Canis Iupus, Drosophila melanogaster, Anopheles gambiae, Aplysia california, Ciona savignyi, Ciona intestinalis, Hemicentrotus pulcherrimus, 20 Giardia lamblia. Gallus gallus. Brachydanio rerio, Xenopus laevis, Xenopus tropicalis, Schistosoma japonicum, Schistosoma mansoni, Encephalitozoon cuniculi, Wuchereria bancrofti, Cavia porcellus, Sus scrofa, Rattus norvegicus, Pneumocystis carinii or Pagrus major proteins as depicted SEQ ID NO: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 25 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 30 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or its homologs is increased, preferably, in one embodment an increase of 35 the fine chemical of at least 100%, 150%, or preferably to at least 200%, 250%, 300%, 350% or 400%, especially prerferably to at least 450%, 500%, 550%, 600% or more is conferred.

[0059.0.0.0] In case the biological activity of the Saccaromyces cerevisiae protein YNL090W as depicted in SEQ ID NO: 2, or the biological activity of the Kluyveromyces

lactis, Cryptococcus neoformans, Neurospora crassa, Penicillium marneffei, Mucor rouxii, Schizophyllum commune, Paracoccidioides brasiliensis, Aspergillus fumigatus, Suillus bovinus, Candida albicans, Trichoderma reesei, Ashbya gossypii, Yarrowia lipolytica, Ustilago maydis, Emericella nidulans, Trichomonas vaginalis, Colletotrichum trifolii, Blumeria graminis, Dictyostelium discoideum, Schizosaccharomyces pombe, 5 Entamoeba histolytica, Oryza sativa, Brassica napus, Glycine max, Beta vulgaris, Lotus japonicus, Zinnia elegans, Zea mays, Cicer arietinum, Arabidopsis thaliana, Hordeum vulgare, Nicotiana tabacum, Gossypium hirsutum, Physcomitrella patens, Fucus distichus, Medicago truncutula, Homo sapiens, Caenorhabditits elegans, Tigriopus japonicus, Rhopalosiphum padi, Mus musculus, Discopyge ommata, Canis 10 lupus, Drosophila melanogaster, Anopheles gambiae, Aplysia california, Ciona savignyi, Ciona intestinalis, Hemicentrotus pulcherrimus, Giardia lamblia, Gallus gallus, Brachydanio rerio, Xenopus laevis, Xenopus tropicalis, Schistosoma japonicum, Schistosoma mansoni, Encephalitozoon cuniculi, Wuchereria bancrofti, Cavia porcellus, Sus scrofa, Rattus norvegicus, Pneumocystis carinii or Pagrus major 15 proteins as depicted SEQ ID NO: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 20 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 25 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or its homologs is increased, preferably, an increase of the fine chemical in conferred, preferably of the fine chemical such as essential amino acids e.g. tryptophane, arginine, phenylalanine, tyrosine, threonine, valine, isoleucine and/or leucine, nonessential amino acids e.g. proline, alanine, glycine or serine, modified amino acids e.g. 30 3,4-dihydroxyphenylalanine, carbohydrates e.g. raffinose, inositol or iso-maltose, vitamins e.g.  $\alpha$ -tocopherol,  $\beta$ -tocopherol or  $\gamma$ -tocopherol, organic acids e.g. ferulic acid, sinapic acid or malate, fatty acids e.g. cerotic acid, lignoceric acid, 2-hydroxy-palmitic acid or stearic acid, carotinoids e.g. β-carotene or mixtures thereof is conferred.

[0060.0.0.0] In this context, the fine chemical amount in a cell, preferably in a tissue, more preferred in a organism as a plant or a microorganim or part thereof, is increased by at least 3%, 4%, 5%, 6%, 7%, 8% or 9% or more, especially preferably are at least 10%, 20%, 40%, 50% or more, very especially preferably are more than 60%, 70%, 80%, 90%, 100% or more and most preferably are 150% or more, such as 200%, 250%, 300%, 350%, 400%, 450%, 500%, 550% or 600%.

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The fine chemical can be contained in the organism either in its free [0061.0.0.0] form and/or bound to proteins, polypeptids or other compounds such as polysaccharides, lipids, glycoproteins or glycolipids etc. or mixtures thereof. Accordingly, in one embodiment, the amount of the free form in a cell, preferably in a tissue, more preferred in a organism as a plant or a microorganim or part thereof, is increased by at least 3%, 4%, 5%, 6%, 7%, 8% or 9% or more, especially preferably are at least 10%, 20%, 40%, 50% or more, very especially preferably are more than 60%, 70%, 80%, 90%, 100% or more and most preferably are 150% or more, such as 200%, 250%, 300%, 350%, 400%, 450%, 500%, 550% or 600%. Accordingly, in an other embodiment, the amount of the bound the fine chemical in a cell, preferably in a tissue, more preferred in a organism as a plant or a microorganism or part thereof, is increased by at least 3%, 4%, 5%, 6%, 7%, 8% or 9% or more, especially preferably are at least 10%, 20%, 40%, 50% or more, very especially preferably are more than 60%, 70%, 80%, 90%, 100% or more and most preferably are 150% or more, such as 200%, 250%, 300%, 350%, 400%, 450%, 500%, 550% or 600%.

[0062.0.0.0] A protein having an activity conferring an increase in the amount or level of the fine chemical preferably has the structure of the polypeptide described herein, in particular of the polypeptides comprising the consensus sequence shown in SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 397, SEQ ID NO: 398, SEQ ID NO: 399 and/or SEQ ID NO: 400 20 as described herein, or is encoded by the nucleic acid molecule characterized herein or the nucleic acid molecule according to the invention, for example by the nucleic acid molecule as shown in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 25 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 30 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 or its herein described functional homologues and has the herein mentioned activity.

35 [0063.0.0.0] For the purposes of the present invention, the terms "the fine chemical" or "fine chemical" such as essential amino acids e.g. tryptophane, arginine, phenylalanine, tyrosine, threonine, valine, isoleucine and/or leucine, non-essential amino acids e.g. proline, alanine, glycine or serine, modified amino acids e.g. 3,4-dihydroxyphenylalanine, carbohydrates e.g. raffinose, inositol or iso-maltose, vitamins e.g. α-tocopherol, β-tocopherol or γ-tocopherol, organic acids e.g. ferulic acid, sinapic acid or malate, fatty acids e.g. cerotic acid, lignoceric acid, 2-hydroxy-palmitic acid or

stearic acid, carotinoids e.g. β-carotene or mixtures thereof also encompass the corresponding salts, such as, for example, tryptophane hydrochloride, arginine hydrochloride, phenylalanine hydrochloride, tyrosine hydrochloride, threonine hydrochloride, valine hydrochloride, isoleucine hydrochloride or leucine hydrochloride or tryptophane sulfate, arginine sulfate, phenylalanine sulfate, tyrosine sulfate, threonine sulfate, valine sulfate, isoleucine sulfate or leucine sulfate; ester or amids.

[0064.0.0.0] Owing to the biological activity of the proteins which are used in the process according to the invention and which are encoded by nucleic acid molecules according to the invention, it is possible to produce compositions comprising the fine chemical, i.e. an increased amount of the free chemical free or bound, e.g amino acid compositions. Depending on the choice of the organism used for the process according to the present invention, for example a microorganism or a plant, compositions or mixtures of various fine chemicals e.g. amino acids can be produced.

[0065.0.0.0] The term "expression" refers to the transcription and/or translation of a codogenic gene segment or gene. As a rule, the resulting product is an mRNA or a protein. However, expression products can also include functional RNAs such as, for example, antisense, nucleic acids, tRNAs, snRNAs, rRNAs, RNAi, siRNA, ribozymes etc. Expression may be systemic, local or temporal, for example limited to certain cell types, tissuesorgans or time periods.

20 [0066.0.0.0] In one embodiment, the process of the present invention comprises one or more of the following steps:

stabilizing a protein conferring the increased expression of a protein encoded by a) the nucleic acid molecule of the invention or of the protein of the invention, e.g. of a protein having the biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 25 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 30. 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 35 380, 382, 384, 386, 388, 390, 392 or 394 or its homologs having the fine chemical increasing activity;

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- b) stabilizing a mRNA conferring the increased expression of a protein encoded by the nucleic acid molecule of the invention, e.g. of a protein having the biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14. 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or its homologs or of an mRNA encoding the polypeptide of the present invention having the fine chemical increasing activity;
- c) increasing the specific activity of a protein conferring the increased expression of a protein encoded by the nucleic acid molecule of the invention or of the protein of the invention having the fine chemical increasing activity, e.g. of a protein 20 having the biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 25 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 30 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or its homologs, or decreasing the inhibitiory regulation of the protein of the invention;
- d) generating or increasing the expression of an endogenous or artificial transcription factor mediating the expression of a protein conferring the increased expression of a protein encoded by the nucleic acid molecule of the invention or of the protein of the invention having the fine chemical increasing activity, e.g. of a polypeptide having the biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120,

122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or its homologs;

- stimulating activity of a protein conferring the increased expression of a protein 10 - e) encoded by the nucleic acid molecule of the present invention or a protein of the present invention having the fine chemical increasing activity, e.g. of a protein having the biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 15 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 20 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or its homologs, by adding one or more exogenous 25 inducing factors to the organismus or parts thereof;
  - expressing a transgenic gene encoding a protein conferring the increased f) expression of a polypeptide (= protein) encoded by the nucleic acid molecule or the protein of the invention, having the fine chemical increasing activity, e.g. of a protein having the biological activity represented by a protein as depicted in SEQ 30 ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 35 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 40

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352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or its homologs;

- increasing the copy number of a gene conferring the increased expression of a g) . nucleic acid molecule encoding a protein encoded by the nucleic acid molecule of the invention or the protein of the invention the fine chemical increasing activity, e.g. of a protein having the biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or its homologs;
- increasing the expression of the endogenous gene encoding the protein of the h) invention, e.g. a protein having the biological activity represented by a protein as 20 depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 25 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 30 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or its homologs, by adding positive expression or removing negative expression elements, e.g. homologous recombination can be used to either introduce positive regulatory elements like for plants the 35S enhancer into the promoter or to remove repressor elements 35 form regulatory regions. Further gene conversion methods can be used to disrupt repressor elements or to enhance to acitivty of positive elements. Positive elements can be randomly introduced in plants by T-DNA or transposon mutagenesis and lines can be identified in which the positive elements have be integrated near to a gene of the invention, the expression of which is thereby 40 enhanced;

i) modulating growth conditions of an organism in such a manner, that the expression or activity of the gene encoding the protein of the invention or the protein itself is enhanced for example microorganisms or plants can be grown under a higher temperature regime leading to an enhanced expression of heat shock proteins, e.g. the heat shock protein of the invention, which can lead an enhanced the fine chemical production; and/or

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- j) selecting of organisms with expecially high activity of the protein of the invention from natural or from mutagenized resources and breeding them into the target organisms, eg the elite crops.
- [0067.0.0.0] Preferably, said mRNA is the nucleic acid molecule of the invention 10 and/or the protein conferring the increased expression of a protein encoded by the nucleic acid molecule of the invention or the polypeptide having the herein mentioned activity, e.g. conferring the increase of the fine chemical after increasing the expression or activity of the encoded polypeptide or having the activity of a polypeptide having biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 15 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 20 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 25 382, 384, 386, 388, 390, 392 or 394 or its homologs.
  - [0068.0.0.0] In general, the amount of mRNA, polynucleotide or nucleic acid molecule in a cell or a compartment of an organism correlates with the amount of encoded protein and thus with the overall activity of the encoded protein in said volume. Said correlation is not always linear, the activity in the volume is dependent on the stability of the molecules, the degradation of the molecules or the presence of activating or inhibiting co-factors. Further, product and educt inhibitions of enzymes are well known and described in textbooks, e.g. Stryer, Biochemistry or Zinser et al. "Enzyminhibitoren"/Enzyme inhibitors".
  - [0069.0.0.0] The activity of the abovementioned proteins and/or poylpeptide encoded by the nucleic acid molecule of the present invention can be increased in various ways. For example, the activity in an organism or in a part thereof, like a cell, is increased via increasing the gene product number, e.g. by increasing the expression rate, like introducing a stronger promoter, or by increasing the stability of the mRNA expressed,

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thus increasing the translation rate, and/or increasing the stability of the gene product, thus reducing the proteins decayed. Further, the activity or turnover of enzymes can be influenced in such a way that a reduction or increase of the reaction rate or a modification (reduction or increase) of the affinity to the substrate results, is reached. A mutation in the catalytic centre of a polypeptide of the invention, e.g. an enzyme, can modulate the turn over rate of the enzyme, e.g. a knock out of an essential amino acid can lead to a reduced or completely knock out activity of the enzyme, or the deletion or mutation of regulator binding sites can reduce a negative regulation like a feedback inhibition (or a substrate inhibition, if the substrate level is also increased). The specific activity of an enzyme of the present invention can be increased such that the turn over rate is increased or the binding of a co-factor is improved. Improving the stability of the encoding mRNA or the protein can also increase the activity of a gene product. The stimulation of the activity is also under the scope of the term "increased activity".

[0070.0.0.0] Moreover, the regulation of the abovementioned nucleic acid sequences may be modified so that gene expression is increased. This can be achieved advantageously by means of heterologous regulatory sequences or by modifying, for example mutating, the natural regulatory sequences which are present. The advantageous methods may also be combined with each other.

[0071.0.0.0] In general, an activity of a gene product in an organism or part thereof, in particular in a plant cell, a plant, or a plant tissue or a part thereof or in a microorganism can be increased by increasing the amount of the specific encoding mRNA or the corresponding protein in said organism or part thereof. "Amount of protein or mRNA" is understood as meaning the molecule number of polypeptides or mRNA molecules in an organism, a tissue, a cell or a cell compartment. "Increase" in the amount of a protein means the quantitative increase of the molecule number of said protein in an organism, a tissue, a cell or a cell compartment or part thereof - for example by one of the methods described herein below - in comparison to a wild type, control or reference.

[0072.0.0.0] The increase in molecule number amounts preferably to at least 1%, preferably to more than 10%, more preferably to 30% or more, especially preferably to 50%, 70% or more, very especially preferably to 100%, most preferably to 500% or more. However, a de novo expression is also regarded as subject of the present invention.

[0073.0.0.0] A modification, i.e. an increase or decrease, can be caused by endogenous or exogenous factors. For example, an increase in activity in an organism or a part thereof can be caused by adding a gene product or a precursor or an activator or an agonist to the media or nutrition or can be caused by introducing said subjects into a organism, transient or stable.

[0074.0.0.0] In one embodiment the increase in the amount of the fine chemical in the organism or a part thereof, e.g. in a cell, a tissue, an organ, an organelle etc., is achived by increasing the endogenous level of the polypeptide of the invention. Accordingly, in an embodiment of the present invention, the present invention relates to a process wherein the gene copy number of a gene encoding the polynucleotide or nucleic acid molecule of the invention is increased. Further, the endogenous level of the polypeptide of the invention can for example be increased by modifying the transcriptional or translational regulation of the polypeptide.

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[0075.0.0.0] In one embodiment the amount of the fine chemical in the organism or part thereof can be increase by targeted or random mutagenesis of the endogenous .. 10 genes of the invention. For example homologous recombination can be used to either introduce positive regulatory elements like for plants the 35S enhancer into the promoter or to remove repressor elements form regulatory regions. In addition gene conversion like methods described by Kochevenko and Willmitzer (Plant Physiol. 2003 May;132(1):174-84) and citations therein can be used to disrupt repressor elements or 15 to enhance to acitivty of positive regulatory elements. Furthermore positive elements can be randomly introduced in (plant) genomes by T-DNA or transposon mutagenesis and lines can be screened for, in which the positive elements has be integrated near to a gene of the invention, the expression of which is thereby enhanced. The activation of plant genes by random integrations of enhancer 20 elements has been described by Hayashi et al., 1992 (Science 258:1350-1353) or Weigel et al., 2000 (Plant Physiol. 122, 1003-1013) and others citated therein. Reverse genetic strategies to identify insertions (which eventually carrying the activation elements) near in genes of interest have been described for various cases 25

activation elements) near in genes of interest have been described for various cases eg. Krysan et al., 1999 (Plant Cell 1999, 11, 2283-2290); Sessions et al., 2002 (Plant Cell 2002, 14, 2985-2994); Young et al., 2001, (Plant Physiol. 2001, 125, 513-518); Koprek et al., 2000 (Plant J. 2000, 24, 253-263); Jeon et al., 2000 (Plant J. 2000, 22, 561-570); Tissier et al., 1999 (Plant Cell 1999, 11, 1841-1852); Speulmann et al., 1999 (Plant Cell 1999, 11, 1853-1866). Briefly material from all plants of a large T-DNA or transposon mutagenized plant population is harvested and genomic DNA prepared. Then the genomic DNA is pooled following specific architectures as described for

Then the genomic DNA is pooled following specific architectures as described for example in Krysan et al., 1999 (Plant Cell 1999, 11, 2283-2290). Pools of genomics DNAs are then screened by specific multiplex PCR reactions detecting the combination of the insertional mutagen (eg T-DNA or Transposon) and the gene of interest.

Therefore PCR reactions are run on the DNA pools with specific combinations of T-DNA or transposon border primers and gene specific primers. General rules for primer design can again be taken from Krysan et al., 1999 (Plant Cell 1999, 11, 2283-2290) Rescreening of lower levels DNA pools lead to the identification of individual plants in which the gene of interest is disrupted by the insertional mutagen.

The enhancement of positive regulatory elements or the disruption or weaking of negative regulatory elements can also be achieved through common mutagenesis

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techniques: The production of chemically or radiation mutated populations is a common technique and known to the skilled worker. Methods for plants are described by Koorneef et al. 1982 and the citations therein and by Lightner and Caspar in "Methods in Molecular Biology" Vol 82. These techniques usually induce pointmutations that can be identified in any known gene using methods such as TILLING (Colbert et al. 2001).

[0076.0.0.0] Accordingly, the expression level can be increased if the endogenous genes encoding a polypeptide conferring an increased expression of the polypeptide of the present invention, in particular genes comprising the nucleic acid molecule of the present invention, are modified via homologous recombination, Tilling approaches or gene conversion.

[0077.0.0.0] Regulatory sequences can be operatively linked to the coding region of an endogenous protein and control its transcription and translation or the stability or decay of the encoding mRNA or the expressed protein. In order to modify and control the expression, promoter, UTRs, splicing sites, processing signals, polyadenylation sites, terminators, enhancers, repressors, post transcriptional or posttranslational modification sites can be changed, added or amended for example, the activation of plant genes by random integrations of enhancer elements has been described by Hayashi et al., 1992 (Science 258:1350-1353) or Weigel et al., 2000 (Plant Physiol. 122, 1003-1013) and others citated therein. For example, the expression level of the endogenous protein can be modulated by replacing the endogenous promoter with a stronger transgenic promoter or by replacing the endogenous 3'UTR with a 3'UTR, which provides more stability without amending the coding region. Further, the transcriptional regulation can be modulated by introduction of an artifical transcription factor as described in the examples. Alternative promoters, terminators and UTR are described below.

[0078.0.0.0] The activation of an endogenous polypeptide having the fine chemical increasing activity, e.g. having the biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394, e.g. conferring the increase of the fine chemical after increase of expression or activity can also be increased by introducing a synthetic transcription factor, which binds close to

the coding region of the protein of the invention encoding gene and activates its transcription. A chimeric zinc finger protein can be construed, which comprises a specific DNA-binding domain and an activation domain as e.g. the VP16 domain of Herpes Simplex virus. The specific binding domain can bind to the regulatory region of the nucleic acid sequence used in the inventive process. The expression of the chimeric transcription factor in an organism, in particular in a plant, leads to a specific expression of the protein of the invention, see e.g. in WO01/52620, Oriz, Proc. Natl. Acad. Sci. USA, 2002, Vol. 99, 13290 or Guan, Proc. Natl. Acad. Sci. USA, 2002, Vol. 99, 13296.

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- [0079.0.0.0] In one further embodiment of the process according to the invention, 10 organisms are used in which one of the abovementioned genes, or one of the abovementioned nucleic acids, is mutated in a way that the activity of the encoded gene products is less influenced by cellular factors, or not at all, in comparison with the unmutated proteins. For example, well known regulation mechanism of enzymic activity are substrate inhibition or feed back regulation mechanisms. Ways and techniques for 15 the introduction of substitutions, deletions and additions of one or more bases, nucleotides or amino acids of a corresponding sequence are described herein below in the corresponding paragraphs and the references listed there, e.g. in Sambrook et al., Molecular Cloning, Cold Spring Habour, NY, 1989. The person skilled in the art will be able to identify regulation domains and binding sites of regulators by comparing the 20 sequence of the nucleic acid molecule of the present invention or the expression product thereof with the state of the art by computer software means which comprise algorithms for the identifying of binding sites and regulation domains or by introducing into a nucleic acid molecule or in a protein systematically mutations and assaying for those mutations which will lead to an increased specifiy activity or an increased activity 25 per volume, in particular per cell.
  - [0080.0.0.0] It is therefore adavantageously to express in an organism a nucleic acid molecule of the invention or a polypeptide of the invention derived from a evolutionary distantly related organism, as e.g. using a prokaryotic gene in a eukaryotic host, as in these cases the regulation mechanism of the host cell may not weaken the activity (cellular or specific) of the gene or its expression product
  - [0081.0.0.0] The mutation is introduced in such a way that the production of the fine chemical is not adversely affected.
  - [0082.0.0.0] Less influence on the regulation of a gene or its gene product is understood as meaning a reduced regulation of the enzymatic activity leading to an increased specific or cellular activity of the gene or its product. An increase of the enzymatic activity is understood as meaning an enzymatic activity, which is increased by at least 10%, 20%, 30%, 40% or 50%, advantageously by at least 60%, 70%, 80%, 90% or 100%, especially advantageously by at least 150%, 200%, 300% or more in

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comparison with the starting organism. In the event the inventive nucleic acid sequences were introduced into an organism, which did not have the encoded protein activity, said new generated enzymatic activity shall also be embraced by the herein described invention. This leads to an increased productivity of the desired fine chemical.

[0083.0.0.0] Owing to the introduction of a gene or a plurality of genes conferring the expression of the nucleic acid molecule of the invention or the polypeptide of the invention as described below, for example the nucleic acid construct mentioned below, or e.g. encoding the protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 into an organism alone or in combination with other genes, it is possible not only to increase the biosynthetic flux towards the end product, but also to increase, modify or create de novo an advantageous, preferably novel metabolites composition in the organism, e.g. an advantageous amino acid composition comprising a higher content of (from a viewpoint of nutrional physiology limited) amino acids, for example essential amino acids like tryptophane, threonine, methionine or lysine.

[0084.0.0.0] Preferably the composition comprises further higher amounts of metabolites positively affecting or lower amounts of metabolites negatively affecting the nutrition or health of animals or humans provided with said compositions or organisms of the invention or parts thereof. Likewise, the number or activity of further genes which are required for the import or export of nutrients or metabolites, including for example amino acids or its precursors, required for the cell's biosynthesis of the fine chemical may be increased so that the concentration of necessary or relevant precursors, cofactors or intermediates within the cell(s) or within the corresponding storage compartments is increased. Owing to the increased or novel generated activity of the polypeptide of the invention or owing to the increased number of nucleic acid sequences of the invention and/or to the modulation of further genes which are involved in the biosynthesis of the fine chemical, e.g. by increasing the acitivty of enzymes synthizing precursors or by destroying the activity of one or more genes which are involved in the breakdown of the fine chemical, it is thereby possible to increase the yield, production and/or production efficiency of the fine chemical in the host organism, such as plants or microorganims.

[0085.0.0.0] Accordingly, in one embodiment, the process according to the invention relates to a process, which comprises:

- a) providing a non-human organism, preferably a microorganism, non-human animal, plant or part, cell or tissue thereof;
- increasing the biological activity represented by a protein as depicted in SEQ ID 5 b) NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 10 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 15 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or of a polypeptide being encoded by the nucleic acid molecule of the invention and described below, i.e. conferring an increase of the fine chemical in the organism, preferably in the microorganism, the nonhuman animal, the plant or part, cell or tissue thereof, 20
  - growing the organism, preferably the microorganism, the non-human animal, the plant or part, cell or tissue thereof under conditions which permit the production of the fine chemical; and
  - d) if desired, revovering, optionally isolating, the free and/or bound fine chemical.
- [0086.0.0.0] The organism, in particular the microorganism, non-human animal, the plant or animal parts, the plant or animal cell, the plant or animal tissue or the plant is advantageously grown in such a way that it is not only possible to recover, if desired isolate the free or bound fine chemical (Galili et al., Transgenic Res., 2000, 9, 2, 137-144).
- [0087.0.0.0] After the above-described increasing (which as defined above also encompasses the generating of an activity in an organism, i.e. a *de novo* activity), for example after the introduction and the expression of the nucleic acid molecules of the invention or described in the methods or processes according to the invention, the organism according to the invention, advantageously, a microorganism, a non-human animal, a plant, plant or animal tissue or plant or animal cell, is grown and subsequently harvested.

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harvested.

[0088.0.0.0] Suitable organisms or host organisms (transgenic organism) for the nucleic acid molecule used according to the invention and for the inventive process, the nucleic acid construct or the vector (both as described below) are, in principle, all organisms which are capable of synthesizing the fine chemical, and which are suitable for the activation, introduction or stimulation genes. Examples which may be mentioned are plants, microorganisms such as fungi, bacteria, yeasts, alga or diatom, transgenic or obtained by site directed mutagenesis or random mutagenesis combined with specific selection procedures. Preferred organisms are those which are naturally capable of synthesizing the fine chemical in substantial amounts, like fungi, yeasts, bactria or plants. In principle, transgenic animals, for example Caenorhabditis elegans, are also suitable as host organisms.

[0089.0.0.0] In the event that the transgenic organism is a microorganism, such as a eukaryotic organism, for example a fungus, an alga, diatom or a yeast in particular a fungus, alga, diatom or yeast selected from the families Chaetomiaceae, Choanephoraceae, Cryptococcaceae, Cunninghamellaceae, Demetiaceae, Dipodascaceae, Moniliaceae, Mortierellaceae, Mucoraceae, Pythiaceae, Saccharomycetaceae, Saprolegniaceae, Schizosaccharomycetaceae, Sodariaceae, Sporobolomycetaceae Tuberculariaceae, Adelotheciaceae, Dinophyceae, Ditrichaceae or Prasinophyceae, or a fungus selected from the families Tremellaceae, Filobasidiaceae, Christianseniaceae, Cystofilobasidiaceae, Sordariaceae, Annulatascaceae, Cephalothecaceae, Chaetomiaceae, Coniochaetaceae, Lasiosphaeriaceae, Pleurotremataceae, Elaphomycetaceae, Trichocomaceae, Mucoraceae, Schizophyllaceae, Onygenaceae, Suillaceae, Hypocreaceae. Ustilaginaceae, Trichocomaceae, Phyllachoraceae, Erysiphaceae or a prokaryotic organism, for example a bacterium or blue alga, in particular a bacterium from the families Actinomycetaceae, Bacillaceae, Brevibacteriaceae, Corynebacteriaceae, Cyanophyceae, Enterobacteriacae, Gordoniaceae, Nocardiaceae, Micrococcaceae, Mycobacteriaceae, Pseudomonaceae, Rhizobiaceae or Streptomycetaceae. this microorganism is grown on a solid or in a liquid medium which is known to the skilled

[0090.0.0.0] The microorganisms or the recovered, and if desired isolated, fine chemical can then be processed further directly into foodstuffs or animal feeds or for other applications, for example according to the disclosures made in EP-B-0 533 039 or EP-A-0 615 693, which are expressly incorporated herein by reference. The fermentation broth or fermentation products can be purified in the customary manner by extraction and precipitation or via ion exchangers and other methods known to the person skilled in the art and described herein below. Products of these different work-up procedures are fine chemical e.g. amino acids or amino acid compositions which still comprise fermentation broth and cell components in different amounts, advantageously in the range of from 0 to 99% by weight, preferably below 80% by

worker and suits the organism. After the growing phase, the organisms can be

weight, especially preferably between below 50%, 40%, 30%, 20%, 10% or 5% by weight.

[0091.0.0.0] Preferred microorganisms are selected from the group consisting of Chaetomiaceae such as the genera Chaetomium e.g. the species Chaetomidium fimeti; Choanephoraceae such as the genera Blakeslea, Choanephora e.g. the species Blakeslea trispora, Choanephora cucurbitarum or Choanephora infundibulifera var. cucurbitarum; Cryptococcaceae such as the genera Candida, Crytococcus, Rhodotorula, Torulopsis e.g. the species Candida albicans, Candida albomarginata, Candida antarctica, Candida bacarum, Candida bogoriensis, Candida boidinii, Candida bovina, Candida brumptii, Candida cacaoi, Candida cariosilignicola, Candida 10 catenulata, Candida chalmersii, Candida ciferrii, Candida cylindracea, Candida edax, Candida ernobii, Candida famata, Candida freyschussii, Candida friedrichii, Candida glabrata, Candida guilliermondii, Candida haemulonii, Candida humicola, Candida inconspicua, Candida ingens, Candida intermedia, Candida kefyr, Candida krusei, Candida lactiscondensi, Candida lambica, Candida lipolytica, Candida lusitaniae, 15 Candida macedoniensis, Candida magnoliae, Candida membranaefaciens, Candida mesenterica, Candida multigemmis, Candida mycoderma, Candida nemodendra, Candida nitratophila, Candida norvegensis, Candida norvegica, Candida parapsilosis, Candida pelliculosa, Candida peltata, Candida pini, Candida pseudotropicalis, Candida pulcherrima, Candida punicea, Candida pustula, Candida ravautii, Candida reukaufii, 20 Candida rugosa, Candida sake, Candida silvicola, Candida solani, Candida sp., Candida spandovensis, Candida succiphila, Candida tropicalis, Candida utilis, Candida valida, Candida versatilis, Candida vini, Candida zeylanoides, Cryptococcus albidus, Cryptococcus curvatus, Cryptococcus flavus, Cryptococcus humicola, Cryptococcus hungaricus, Cryptococcus kuetzingii, Cryptococcus laurentii, Cryptococcus macerans, 25 Cryptococcus neoformans, Cryptococcus terreus, Cryptococcus uniguttulatus, Rhodotorula acheniorum, Rhodotorula bacarum, Rhodotorula bogoriensis, Rhodotorula flava, Rhodotorula glutinis, Rhodotorula macerans, Rhodotorula minuta, Rhodotorula mucilaginosa, Rhodotorula pilimanae, Rhodotorula pustula, Rhodotorula rubra, Rhodotorula tokyoensis, Torulopsis colliculosa, Torulopsis dattila or Torulopsis 30 neoformans; Cunninghamellaceae such as the genera Cunninghamella e.g. the species Cunninghamella blakesleeana, Cunninghamella echinulata, Cunninghamella echinulata var. elegans, Cunninghamella elegans or Cunninghamella homothallica; Demetiaceae such as the genera Alternaria, Bipolaris, Cercospora, Chalara, Cladosporium, Curvularia, Exophilia, Helicosporium, Helminthosporium, Orbimyces, 35 Philalophora, Pithomyces, Spilocaea, Thielaviopsis, Wangiella e.g. the species Curvularia affinis, Curvularia clavata, Curvularia fallax, Curvularia inaequalis, Curvularia indica, Curvularia lunata, Curvularia pallescens, Curvularia verruculosa or Helminothosporium sp.; Moniliaceae such as the genera Arthrobotrys, Aspergillus, Epidermophyton, Geotrichum, Gliocladium, Histoplasma, Microsporum, Monilia, 40 Oedocephalum, Oidium, Penicillium, Trichoderma, Trichophyton, Thrichoteclum,

34 Verticillium e.g. the species Aspergillus aculeatus, Aspergillus albus, Aspergillus alliaceus. Aspergillus asperescens , Aspergillus awamori, Aspergillus candidus, Aspergillus carbonarius, Aspergillus carneus, Aspergillus chevalieri, Aspergillus chevalieri var. intermedius, Aspergillus clavatus, Aspergillus ficuum, Aspergillus flavipes, Aspergillus flavus, Aspergillus foetidus, Aspergillus fumigatus, Aspergillus giganteus, Aspergillus humicola, Aspergillus intermedius, Aspergillus japonicus, Aspergillus nidulans, Aspergillus niger, Aspergillus niveus, Aspergillus ochraceus, Aspergillus oryzae, Aspergillus ostianus, Aspergillus parasiticus, Aspergillus parasiticus var. globosus, Aspergillus penicillioides, Aspergillus phoenicis, Aspergillus rugulosus, Aspergillus sclerotiorum, Aspergillus sojae var. gymnosardae, Aspergillus sydowi, 10 Aspergillus tamarii, Aspergillus terreus, Aspergillus terricola, Aspergillus toxicarius, Aspergillus unguis, Aspergillus ustus, Aspergillus versicolor, Aspergillus vitricolae, Aspergillus wentii, Penicillium adametzi, Penicillium albicans, Penicillium arabicum, Penicillium arenicola, Penicillium argillaceum, Penicillium arvense, Penicillium asperosporum. ·Penicillium aurantiogriseum, ·Penicillium avellaneum, ·Penicillium 15 baarnense, Penicillium bacillisporum, Penicillium brasilianum, Penicillium brevicompactum, Penicillium camemberti, Penicillium canadense, Penicillium canescens. Penicillium caperatum, Penicillium capsulatum, Penicillium caseicolum, Penicillium chrysogenum, Penicillium citreonigrum, Penicillium citrinum. Penicillium claviforme. Penicillium commune, Penicillium 20 corylophilum, ·Penicillium corymbiferum, ·Penicillium crustosum, ·Penicillium cyclopium, Penicillium daleae, Penicillium decumbens, Penicillium dierckxii, Penicillium digitatum, Penicillium digitatum var. latum, Penicillium divaricatum, Penicillium diversum. Penicillium duclauxii, Penicillium echinosporum, Penicillium expansum, ·Penicillium fellutanum, ·Penicillium frequentans, ·Penicillium 25 funiculosum. Penicillium glabrum. Penicillium gladioli, Penicillium griseofulvum, Penicillium hirsutum, Penicillium hispanicum, Penicillium islandicum, Penicillium italicum, Penicillium italicum var. avellaneum, Penicillium janczewskii, Penicillium janthinellum, Penicillium japonicum, Penicillium lavendulum, Penicillium lilacinum, Penicillium lividum, Penicillium martensii, Penicillium 30 megasporum, Penicillium miczynskii, Penicillium nalgiovense, Penicillium nigricans, Penicillium notatum, Penicillium ochrochloron, Penicillium odoratum, Penicillium oxalicum, Penicillium paraherquei, Penicillium patulum, Penicillium pinophilum, Penicillium piscarium, Penicillium pseudostromaticum, Penicillium puberulum, Penicillium purpurogenum, Penicillium 35 raciborskii, Penicillium roqueforti, Penicillium rotundum. Penicillium rubrum, Penicillium sacculum, Penicillium simplicissimum, Penicillium sp., Penicillium spinulosum, Penicillium steckii, Penicillium stoloniferum, Penicillium striatisporum, Penicillium striatum, Penicillium tardum, Penicillium thomii, Penicillium turbatum, Penicillium

variabile, Penicillium vermiculatum, Penicillium vermoesenii, Penicillium verrucosum, 40 Penicillium verrucosum var. corymbiferum, Penicillium verrucosum var. cyclopium, Penicillium verruculosum, Penicillium vinaceum, Penicillium violaceum, Penicillium

viridicatum, Penicillium vulpinum, Trichoderma hamatum, Trichoderma harzianum, Trichoderma koningii, Trichoderma longibrachiatum, Trichoderma polysporum, Trichoderma reesei, Trichoderma virens or Trichoderma viride; Mortierellaceae such as the genera Mortierella e.g. the species Mortierella isabellina, Mortierella polycephala, Mortierella ramanniana, Mortierella vinacea or Mortierella zonata; Mucoraceae such as 5 the genera Actinomucor, Mucor, Phycomyces, Rhizopus, Zygorhynchus e.g. the species Mucor amphibiorum, Mucor circinelloides f. circinelloides, Mucor circinelloides var. griseocyanus, Mucor flavus, Mucor fuscus, Mucor griseocyanus, Mucor heterosporus, Mucor hiemalis, Mucor hiemalis f. hiemalis, Mucor inaequisporus, Mucor indicus, Mucor javanicus, Mucor mucedo, Mucor mucilagineus, Mucor piriformis, Mucor 10 plasmaticus, Mucor plumbeus, Mucor racemosus, Mucor racemosus f. racemosus, Mucor racemosus f. sphaerosporus, Mucor rouxianus, Mucor rouxii, Mucor sinensis, Mucor sp., Mucor spinosus, Mucor tuberculisporus, Mucor variisporus, Mucor variosporus, Mucor wosnessenskii, Phycomyces blakesleeanus, Rhizopus achlamydosporus, Rhizopus arrhizus, Rhizopus chinensis, Rhizopus delemar, 15 Rhizopus formosaensis, Rhizopus japonicus, Rhizopus javanicus, Rhizopus microsporus, Rhizopus microsporus var. chinensis, Rhizopus microsporus var. oligosporus, Rhizopus microsporus var. rhizopodiformis, Rhizopus nigricans, Rhizopus niveus, Rhizopus oligosporus, Rhizopus oryzae, Rhizopus pygmaeus, Rhizopus rhizopodiformis, Rhizopus semarangensis, Rhizopus sontii, Rhizopus stolonifer, 20 Rhizopus thermosus, Rhizopus tonkinensis, Rhizopus tritici or Rhizopus usamii; Pythiaceae such as the genera Phytium, Phytophthora e.g. the species Pythium debaryanum, Pythium intermedium, Pythium irregulare, Pythium megalacanthum, Pythium paroecandrum, Pythium sylvaticum, Pythium ultimum, Phytophthora cactorum, Phytophthora cinnamomi, Phytophthora citricola, Phytophthora citrophthora, 25 Phytophthora cryptogea, Phytophthora drechsleri, Phytophthora erythroseptica, Phytophthora lateralis, Phytophthora megasperma, Phytophthora nicotianae, Phytophthora nicotianae var. parasitica, Phytophthora palmivora, Phytophthora parasitica or Phytophthora syringae; Saccharomycetaceae such as the genera Hansenula, Pichia, Saccharomyces, Saccharomycodes, Yarrowia e.g. the species 30 Hansenula anomala, Hansenula californica, Hansenula canadensis, Hansenula capsulata, Hansenula ciferrii, Hansenula glucozyma, Hansenula henricii, Hansenula holstii, Hansenula minuta, Hansenula nonfermentans, Hansenula philodendri, Hansenula polymorpha, Hansenula saturnus, Hansenula subpelliculosa, Hansenula wickerhamii, Hansenula wingei, Pichia alcoholophila, Pichia angusta, Pichia anomala, 35 Pichia bispora, Pichia burtonii, Pichia canadensis, Pichia capsulata, Pichia carsonii, Pichia cellobiosa, Pichia ciferrii, Pichia farinosa, Pichia fermentans, Pichia finlandica, Pichia glucozyma, Pichia guilliermondii, Pichia haplophila, Pichia henricii, Pichia holstii,

Pichia jadinii, Pichia lindnerii, Pichia membranaefaciens, Pichia methanolica, Pichia minuta var. minuta, Pichia minuta var. nonfermentans, Pichia norvegensis, Pichia

ohmeri, Pichia pastoris, Pichia philodendri, Pichia pini, Pichia polymorpha, Pichia

quercuum, Pichia rhodanensis, Pichia sargentensis, Pichia stipitis, Pichia

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strasburgensis, Pichia subpelliculosa, Pichia toletana, Pichia trehalophila, Pichia vini, Pichia xylosa, Saccharomyces aceti, Saccharomyces bailii, Saccharomyces bayanus, Saccharomyces bisporus, Saccharomyces capensis, Saccharomyces carlsbergensis, Saccharomyces cerevisiae, Saccharomyces cerevisiae var. ellipsoideus,

- Saccharomyces chevalieri, Saccharomyces delbrueckii, Saccharomyces diastaticus, Saccharomyces drosophilarum, Saccharomyces elegans, Saccharomyces ellipsoideus, Saccharomyces fermentati, Saccharomyces florentinus, Saccharomyces fragilis, Saccharomyces heterogenicus, Saccharomyces hienipiensis, Saccharomyces inusitatus, Saccharomyces italicus, Saccharomyces kluyveri, Saccharomyces krusei,
- 10 Saccharomyces lactis, Saccharomyces marxianus, Saccharomyces microellipsoides, Saccharomyces montanus, Saccharomyces norbensis, Saccharomyces oleaceus, Saccharomyces paradoxus, Saccharomyces pastorianus, Saccharomyces pretoriensis, Saccharomyces rosei, Saccharomyces rouxii, Saccharomyces uvarum, Saccharomycodes ludwigii or Yarrowia lipolytica; Saprolegniaceae such as the genera
- 15 Saprolegnia e.g. the species Saprolegnia ferax; Schizosaccharomycetaceae such as the genera Schizosaccharomyces e.g. the species Schizosaccharomyces japonicus var. japonicus, Schizosaccharomyces japonicus var. versatilis, Schizosaccharomyces malidevorans, Schizosaccharomyces octosporus, Schizosaccharomyces pombe var. malidevorans or Schizosaccharomyces pombe var. pombe; Sodariaceae such as the
- genera Neurospora, Sordaria e.g. the species Neurospora africana, Neurospora crassa, Neurospora intermedia, Neurospora sitophila, Neurospora tetrasperma, Sordaria fimicola or Sordaria macrospora; Tuberculariaceae such as the genera Epicoccum, Fusarium, Myrothecium, Sphacelia, Starkeyomyces, Tubercularia e.g. the species Fusarium acuminatum, Fusarium anthophilum, Fusarium aquaeductuum,
- Fusarium aquaeductuum var. medium, Fusarium avenaceum, Fusarium buharicum, Fusarium camptoceras, Fusarium cerealis, Fusarium chlamydosporum, Fusarium ciliatum, Fusarium coccophilum, Fusarium coeruleum, Fusarium concolor, Fusarium crookwellense, Fusarium culmorum, Fusarium dimerum, Fusarium diversisporum, Fusarium equiseti, Fusarium equiseti var. bullatum, Fusarium eumartii, Fusarium
- 30 flocciferum, Fusarium fujikuroi, Fusarium graminearum, Fusarium graminum, Fusarium heterosporum, Fusarium incarnatum, Fusarium inflexum, Fusarium javanicum, Fusarium lateritium, Fusarium lateritium var. majus, Fusarium longipes, Fusarium melanochlorum, Fusarium merismoides, Fusarium merismoides var. chlamydosporale, Fusarium moniliforme, Fusarium moniliforme var. anthophilum, Fusarium moniliforme var. subglutinans, Fusarium nivale, Fusarium nivale var. majus, Fusarium oxysporum,
  - Fusarium oxysporum f. sp. aechmeae, Fusarium oxysporum f. sp. cepae, Fusarium oxysporum f. sp. conglutinans, Fusarium oxysporum f. sp. cucumerinum, Fusarium oxysporum f. sp. cucumerinum, Fusarium oxysporum f. sp. dianthi, Fusarium oxysporum f. sp. lycopersici, Fusarium oxysporum f. sp. melonis, Fusarium oxysporum f. sp.
- passiflorae, Fusarium oxysporum f. sp. pisi, Fusarium oxysporum f. sp. tracheiphilum, Fusarium oxysporum f. sp. tuberosi, Fusarium oxysporum f. sp. tulipae, Fusarium oxysporum f. sp. vasinfectum, Fusarium pallidoroseum, Fusarium poae, Fusarium

proliferatum, Fusarium proliferatum var. minus, Fusarium redolens, Fusarium redolens f. sp. dianthi, Fusarium reticulatum, Fusarium roseum, Fusarium sacchari var. elongatum, Fusarium sambucinum, Fusarium sambucinum var. coeruleum, Fusarium semitectum, Fusarium semitectum var. majus, Fusarium solani, Fusarium solani f. sp. pisi, Fusarium sporotrichioides, Fusarium sporotrichioides var. minus, Fusarium subjunatum, Fusarium succisae. Fusarium sulphureum, Fusarium tabacinum, Fusarium

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- sublunatum, Fusarium succisae, Fusarium sulphureum, Fusarium tabacinum, Fusarium tricinctum, Fusarium udum, Fusarium ventricosum, Fusarium verticillioides, Fusarium xylarioides or Fusarium zonatum; Sporobolomycetaceae such as the genera Bullera, Sporobolomyces, Itersonilia e.g. the species Sporobolomyces holsaticus,
- Sporobolomyces odorus, Sporobolomyces puniceus, Sporobolomyces salmonicolor, Sporobolomyces singularis or Sporobolomyces tsugae; Adelotheciaceae such as the genera e.g. the species *Physcomitrella patens*; Dinophyceae such as the genera Crypthecodinium, Phaeodactylum e.g. the species *Crypthecodinium cohnii or Phaeodactylum tricornutum*; Ditrichaceae such as the genera Ceratodon, Pleuridium,
- Astomiopsis, Ditrichum, Philibertiella, Ceratodon, Distichium, Skottsbergia e.g. the species Ceratodon antarcticus, Ceratodon purpureus, Ceratodon purpureus ssp. convolutes or Ceratodon purpureus ssp. stenocarpus; Prasinophyceae such as the genera Nephroselmis, Prasinococcus, Scherffelia, Tetraselmis, Mantoniella, Ostreococcus e.g. the species Nephroselmis olivacea, Prasinococcus capsulatus,
- 20 Scherffelia dubia, Tetraselmis chui, Tetraselmis suecica, Mantoniella squamata or Ostreococcus tauri; Actinomycetaceae such as the genera Actinomyces, Actinobaculum, Arcanobacterium, Mobiluncus e.g. the species Actinomyces bernardiae, Actinomyces bovis, Actinomyces bowdenii, Actinomyces canis, Actinomyces cardiffensis, Actinomyces catuli, Actinomyces coleocanis, Actinomyces
- denticolens, Actinomyces europaeus, Actinomyces funkei, Actinomyces georgiae, Actinomyces gerencseriae, Actinomyces hordeovulneris, Actinomyces howellii, Actinomyces humiferus, Actinomyces hyovaginalis, Actinomyces israelii, Actinomyces marimammalium, Actinomyces meyeri, Actinomyces naeslundii, Actinomyces nasicola, Actinomyces neuii subsp. anitratus, Actinomyces neuii subsp. neuii, Actinomyces naicola, Actinomyces naeslundiis.
- odontolyticus, Actinomyces oricola, Actinomyces pyogenes, Actinomyces radicidentis, Actinomyces radingae, Actinomyces slackii, Actinomyces suimastitidis, Actinomyces suis, Actinomyces turicensis, Actinomyces urogenitalis, Actinomyces vaccimaxillae, Actinomyces viscosus, Actinobaculum schaalii, Actinobaculum suis, Actinobaculum urinale, Arcanobacterium bernardiae, Arcanobacterium haemolyticum,
- Arcanobacterium hippocoleae, Arcanobacterium phocae, Arcanobacterium pluranimalium, Arcanobacterium pyogenes, Mobiluncus curtisii subsp. curtisii, Mobiluncus curtisii subsp. holmesii or Mobiluncus mulieris; Bacillaceae such as the genera Amphibacillus, Anoxybacillus, Bacillus, Exiguobacterium, Gracilibacillus, Holobacillus, Saccharococcus, Salibacillus, Virgibacillus e.g. the species Amphibacillus fermentum, Amphibacillus tropicus, Amphibacillus xylanus, Anoxybacillus flavithermus,
- Anoxybacillus gonensis, Anoxybacillus pushchinoensis, Bacillus acidocaldarius,
  Bacillus acidoterrestris, Bacillus aeolius, Bacillus agaradhaerens, Bacillus agri, Bacillus

38 alcalophilus, Bacillus alginolyticus, Bacillus alvei, Bacillus amyloliquefaciens, Bacillus amylolyticus, Bacillus aneurinilyticus, Bacillus aquimaris, Bacillus arseniciselenatis, Bacillus atrophaeus, Bacillus azotofixans, Bacillus azotoformans, Bacillus badius, Bacillus barbaricus, Bacillus benzoevorans, Bacillus borstelensis, Bacillus brevis, Bacillus carboniphilus, Bacillus centrosporus, Bacillus cereus, Bacillus chitinolyticus, .5 Bacillus chondroitinus, Bacillus choshinensis, Bacillus circulans, Bacillus clarkii, Bacillus clausii, Bacillus coagulans, Bacillus cohnii, Bacillus curdlanolyticus, Bacillus cycloheptanicus, Bacillus decolorationis, Bacillus dipsosauri, Bacillus edaphicus, Bacillus ehimensis, Bacillus endophyticus, Bacillus fastidiosus, Bacillus firmus, Bacillus flexus, Bacillus formosus, Bacillus fumarioli, Bacillus funiculus, Bacillus fusiformis, 10 Bacillus sphaericus subsp. fusiformis, Bacillus galactophilus, Bacillus globisporus, Bacillus globisporus subsp. marinus, Bacillus glucanolyticus, Bacillus gordonae, Bacillus halmapalus, Bacillus haloalkaliphilus, Bacillus halodenitrificans, Bacillus halodurans, Bacillus halophilus, Bacillus horikoshii, Bacillus horti, Bacillus infernos, Bacillus insolitus, Bacillus jeotgali, Bacillus kaustophilus, Bacillus kobensis, Bacillus 15 krulwichiae, Bacillus laevolacticus, Bacillus larvae, Bacillus laterosporus, Bacillus lautus, Bacillus lentimorbus, Bacillus lentus, Bacillus licheniformis, Bacillus luciferensis, Bacillus macerans, Bacillus macquariensis, Bacillus marinus, Bacillus marisflavi, Bacillus marismortui, Bacillus megaterium, Bacillus methanolicus, Bacillus migulanus, 20 Bacillus mojavensis, Bacillus mucilaginosus, Bacillus mycoides, Bacillus naganoensis, Bacillus nealsonii, Bacillus neidei, Bacillus niacini, Bacillus okuhidensis, Bacillus oleronius, Bacillus pabuli, Bacillus pallidus, Bacillus pantothenticus, Bacillus parabrevis, Bacillus pasteurii, Bacillus peoriae, Bacillus polymyxa, Bacillus popilliae, Bacillus pseudalcaliphilus, Bacillus pseudofirmus, Bacillus pseudomycoides, Bacillus psychrodurans, Bacillus psychrophilus, Bacillus psychrosaccharolyticus, Bacillus 25 psychrotolerans, Bacillus pulvifaciens, Bacillus pumilus, Bacillus pycnus, Bacillus reuszeri, Bacillus salexigens, Bacillus schlegelii, Bacillus selenitireducens, Bacillus silvestris, Bacillus simplex, Bacillus siralis, Bacillus smithii, Bacillus sonorensis, Bacillus sphaericus, Bacillus sporothermodurans, Bacillus stearothermophilus , Bacillus subterraneus, Bacillus subtilis subsp. spizizenii, Bacillus subtilis subsp. subtilis, Bacillus 30 thermantarcticus, Bacillus thermoaerophilus, Bacillus thermoamylovorans, Bacillus thermoantarcticus, Bacillus thermocatenulatus, Bacillus thermocloacae, Bacillus thermodenitrificans, Bacillus thermoglucosidasius, Bacillus thermoleovorans, Bacillus thermoruber, Bacillus thermosphaericus, Bacillus thiaminolyticus, Bacillus 35 thuringiensis, Bacillus tusciae, Bacillus validus, Bacillus vallismortis, Bacillus vedderi, Bacillus vulcani, Bacillus weihenstephanensis, Exiguobacterium acetylicum, Exiguobacterium antarcticum, Exiguobacterium aurantiacum, Exiguobacterium undae, Gracilibacillus dipsosauri, Gracilibacillus halotolerans, Halobacillus halophilus, Halobacillus karajensis, Halobacillus litoralis, Halobacillus salinus, Halobacillus

40 trueperi, Saccharococcus caldoxylosilyticus, Saccharococcus thermophilus, Salibacillus marismortui, Salibacillus salexigens, Virgibacillus carmonensis, Virgibacillus marismortui, Virgibacillus necropolis, Virgibacillus pantothenticus,

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39 Virgibacillus picturae, Virgibacillus proomii or Virgibacillus salexigens, Brevibacteriaceae such as the genera Brevibacterium e.g. the species Brevibacterium acetylicum, Brevibacterium albidum, Brevibacterium ammoniagenes, Brevibacterium avium, Brevibacterium casei, Brevibacterium citreum, Brevibacterium divaricatum, Brevibacterium epidermidis, Brevibacterium fermentans, Brevibacterium frigoritolerans, Brevibacterium halotolerans, Brevibacterium imperiale, Brevibacterium incertum, Brevibacterium iodinum, Brevibacterium linens, Brevibacterium liquefaciens, Brevibacterium lutescens, Brevibacterium luteum, Brevibacterium lyticum, Brevibacterium mcbrellneri, Brevibacterium otitidis, Brevibacterium oxydans, Brevibacterium paucivorans, Brevibacterium protophormiae, Brevibacterium pusillum, Brevibacterium saperdae, Brevibacterium stationis, Brevibacterium testaceum or Brevibacterium vitaeruminis; Corynebacteriaceae such as the genera Corynebacterium e.g. the species Corynebacterium accolens, Corynebacterium afermentans subsp. afermentans, Corynebacterium afermentans subsp. lipophilum, Corynebacterium ammoniagenes, Corynebacterium amycolatum, Corynebacterium appendicis, Corynebacterium aquilae, Corynebacterium argentoratense, Corynebacterium atypicum, Corynebacterium aurimucosum, Corynebacterium auris, Corynebacterium auriscanis, Corynebacterium betae, Corynebacterium beticola, Corynebacterium bovis, Corynebacterium callunae, Corynebacterium camporealensis, Corynebacterium capitovis, Corynebacterium casei, Corynebacterium confusum, Corynebacterium coyleae, Corynebacterium cystitidis, Corynebacterium durum, Corynebacterium efficiens, Corynebacterium equi, Corynebacterium falsenii, Corynebacterium fascians, Corynebacterium felinum, Corynebacterium flaccumfaciens, Corynebacterium flavescens, Corynebacterium freneyi, Corynebacterium glaucum, Corynebacterium glucuronolyticum, Corynebacterium glutamicum, Corynebacterium hoagii, 25 Corynebacterium ilicis, Corynebacterium imitans, Corynebacterium insidiosum, Corynebacterium iranicum, Corynebacterium jeikeium, Corynebacterium kroppenstedtii, Corynebacterium kutscheri, Corynebacterium lilium, Corynebacterium lipophiloflavum, Corynebacterium macginleyi, Corynebacterium mastitidis, Corynebacterium matruchotii, Corynebacterium michiganense, Corynebacterium 30 michiganense subsp. tessellarius, Corynebacterium minutissimum, Corynebacterium mooreparkense, Corynebacterium mucifaciens, Corynebacterium mycetoides, Corynebacterium nebraskense, Corynebacterium oortii, Corynebacterium paurometabolum, Corynebacterium phocae, Corynebacterium pilosum, Corynebacterium poinsettiae, Corynebacterium propinquum, Corynebacterium 35 pseudodiphtheriticum, Corynebacterium pseudotuberculosis, Corynebacterium

pyogenes, Corynebacterium rathayi, Corynebacterium renale, Corynebacterium riegelii, Corynebacterium seminale, Corynebacterium sepedonicum, Corynebacterium simulans, Corynebacterium singulare, Corynebacterium sphenisci, Corynebacterium spheniscorum, Corynebacterium striatum, Corynebacterium suicordis, 40 Corynebacterium sundsvallense, Corynebacterium terpenotabidum, Corynebacterium testudinoris, Corynebacterium thomssenii, Corynebacterium tritici, Corynebacterium

ulcerans, Corynebacterium urealyticum, Corynebacterium variabile, Corynebacterium vitaeruminis or Corynebacterium xerosis; Enterobacteriacae such as the genera Alterococcus, Arsenophonus, Brenneria, Buchnera, Budvicia, Buttiauxella, Calymmatobacterium, Cedecea, Citrobacter, Edwardsiella, Enterobacter, Erwinia,

- Escherichia, Ewingella, Hafnia, Klebsiella, Kluyvera, Leclercia, Leminorella, Moellerella, Morganella, Obesumbacterium, Pantoea, Pectobacterium, Photorhabdus, Plesiomonas, Pragia, Proteus, Providencia, Rahnella, Saccharobacter, Salmonella, Shigella, Serratia, Sodalis, Tatumella, Trabulsiella, Wigglesworthia, Xenorhabdus, Yersinia and Yokenella e.g. the species *Arsenophonus nasoniae*,
- Brenneria alni, Brenneria nigrifluens, Brenneria quercina, Brenneria rubrifaciens,
  Brenneria salicis, Budvicia aquatica, Buttiauxella agrestis, Buttiauxella brennerae,
  Buttiauxella ferragutiae, Buttiauxella gaviniae, Buttiauxella izardii, Buttiauxella
  noackiae, Buttiauxella warmboldiae, Cedecea davisae, Cedecea lapagei, Cedecea
  neteri, Citrobacter amalonaticus, Citrobacter diversus, Citrobacter freundii, Citrobacter
  genomospecies, Citrobacter gillenii, Citrobacter intermedium, Citrobacter koseri,
  Citrobacter murliniae, Citrobacter sp., Edwardsiella hoshinae, Edwardsiella ictaluri,
- Edwardsiella tarda, Erwinia alni, Erwinia amylovora, Erwinia ananatis, Erwinia aphidicola, Erwinia billingiae, Erwinia cacticida, Erwinia cancerogena, Erwinia carnegieana, Erwinia carotovora subsp. atroseptica, Erwinia carotovora subsp. betavasculorum, Erwinia carotovora subsp. odorifera, Erwinia carotovora subsp. wasabiae, Erwinia chrysanthemi, Erwinia cypripedii, Erwinia dissolvens, Erwinia

herbicola, Erwinia mallotivora, Erwinia milletiae, Erwinia nigrifluens, Erwinia nimipressuralis, Erwinia persicina, Erwinia psidii, Erwinia pyrifoliae, Erwinia quercina, Erwinia rhapontici, Erwinia rubrifaciens, Erwinia salicis, Erwinia stewartii, Erwinia tracheiphila, Erwinia uredovora, Escherichia adecarboxylata, Escherichia anindolica, Escherichia aurescens, Escherichia blattae, Escherichia coli, Escherichia coli var. communior, Escherichia coli-mutabile, Escherichia fergusonii, Escherichia hermannii,

Escherichia sp., Escherichia vulneris, Ewingella americana, Hafnia alvei, Klebsiella aerogenes, Klebsiella edwardsii subsp. atlantae, Klebsiella ornithinolytica, Klebsiella oxytoca, Klebsiella planticola, Klebsiella pneumoniae, Klebsiella pneumoniae subsp. pneumoniae, Klebsiella sp., Klebsiella terrigena, Klebsiella trevisanii, Kluyvera ascorbata, Kluyvera citrophila, Kluyvera cochleae, Kluyvera cryocrescens, Kluyvera georgiana, Kluyvera noncitrophila, Kluyvera sp., Leclercia adecarboxylata, Leminorella grimontii, Leminorella richardii, Moellerella wisconsensis, Morganella morganii,

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Morganella morganii subsp. morganii, Morganella morganii subsp. sibonii,
Obesumbaterium proteus, Pantoea agglomerans, Pantoea ananatis, Pantoea citrea,
Pantoea dispersa, Pantoea punctata, Pantoea stewartii subsp. stewartii, Pantoea
terrea, Pectobacterium atrosepticum, Pectobacterium carotovorum subsp.
atrosepticum, Pectobacterium carotovorum subsp. carotovorum, Pectobacterium

40 chrysanthemi, Pectobacterium cypripedii, Photorhabdus asymbiotica, Photorhabdus luminescens, Photorhabdus luminescens subsp. akhurstii, Photorhabdus luminescens subsp. laumondii, Photorhabdus luminescens subsp. luminescens, Photorhabdus sp.,

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41 Photorhabdus temperata, Plesiomonas shigelloides, Pragia fontium, Proteus hauseri, Proteus ichthyosmius, Proteus inconstans, Proteus mirabilis, Proteus morganii, Proteus myxofaciens, Proteus penneri, Proteus rettgeri, Proteus shigelloides, Proteus vulgaris, Providencia alcalifaciens, Providencia friedericiana, Providencia heimbachae, Providencia rettgeri, Providencia rustigianii, Providencia stuartii, Rahnella aquatilis, Salmonella abony, Salmonella arizonae, Salmonella bongori, Salmonella choleraesuis subsp. arizonae, Salmonella choleraesuis subsp. bongori, Salmonella choleraesuis subsp. cholereasuis, Salmonella choleraesuis subsp. diarizonae, Salmonella choleraesuis subsp. houtenae, Salmonella choleraesuis subsp. indica, Salmonella choleraesuis subsp. salamae, Salmonella daressalaam, Salmonella enterica subsp. - houtenae, Salmonella enterica subsp. salamae, Salmonella enteritidis, Salmonella gallinarum, Salmonella heidelberg, Salmonella panama, Salmonella senftenberg, Salmonella typhimurium, Serratia entomophila, Serratia ficaria, Serratia fonticola, Serratia grimesii, Serratia liquefaciens, Serratia marcescens, Serratia marcescens subsp. marcescens, Serratia marinorubra, Serratia odorifera, Serratia plymouthensis, Serratia plymuthica, Serratia proteamaculans, Serratia proteamaculans subsp. quinovora, Serratia quinivorans, Serratia rubidaea, Shigella boydii, Shigella flexneri, Shigella paradysenteriae, Shigella sonnei, Tatumella ptyseos, Xenorhabdus beddingii, Xenorhabdus bovienii, Xenorhabdus luminescens, Xenorhabdus nematophila, Xenorhabdus nematophila subsp. beddingii, Xenorhabdus nematophila subsp. bovienii, Xenorhabdus nematophila subsp. poinarii or Xenorhabdus poinarii; Gordoniaceae such as the genera Gordonia, Skermania e.g. the species Gordonia aichiensis, Gordonia alkanivorans, Gordonia amarae, Gordonia amicalis, Gordonia bronchialis, Gordonia desulfuricans, Gordonia hirsuta, Gordonia hydrophobica, Gordonia namibiensis, Gordonia nitida, Gordonia paraffinivorans, Gordonia polyisoprenivorans, Gordonia rhizosphera, Gordonia rubripertincta, Gordonia sihwensis, Gordonia sinesedis, Gordonia sputi, Gordonia terrae or Gordonia westfalica; Micrococcaceae such as the genera Micrococcus, Arthrobacter, Kocuria, Nesterenkonia, Renibacterium, Rothia, Stomatococcus e.g. the species Micrococcus agilis, Micrococcus antarcticus, Micrococcus halobius, Micrococcus kristinae, Micrococcus luteus, Micrococcus lylae, Micrococcus nishinomiyaensis, Micrococcus roseus, Micrococcus sedentarius, Micrococcus varians, Arthrobacter agilis, Arthrobacter albus, Arthrobacter atrocyaneus, Arthrobacter aurescens, Arthrobacter chlorophenolicus, Arthrobacter citreus, Arthrobacter creatinolyticus, Arthrobacter crystallopoietes, Arthrobacter cumminsii, Arthrobacter duodecadis, Arthrobacter flavescens, Arthrobacter flavus, Arthrobacter gandavensis, Arthrobacter globiformis, Arthrobacter histidinolovorans, Arthrobacter ilicis, Arthrobacter koreensis, Arthrobacter luteolus, Arthrobacter methylotrophus, Arthrobacter mysorens, Arthrobacter nasiphocae, Arthrobacter nicotianae, Arthrobacter

nicotinovorans, Arthrobacter oxydans, Arthrobacter pascens, Arthrobacter picolinophilus, Arthrobacter polychromogenes, Arthrobacter protophormiae, 40 Arthrobacter psychrolactophilus, Arthrobacter radiotolerans, Arthrobacter ramosus, Arthrobacter rhombi, Arthrobacter roseus, Arthrobacter siderocapsulatus, Arthrobacter

simplex, Arthrobacter sulfonivorans, Arthrobacter sulfureus, Arthrobacter terregens, Arthrobacter tumescens, Arthrobacter uratoxydans, Arthrobacter ureafaciens, Arthrobacter variabilis, Arthrobacter viscosus, Arthrobacter woluwensis, Kocuria erythromyxa, Kocuria kristinae, Kocuria palustris, Kocuria polaris, Kocuria rhizophila, 5 Kocuria rosea, Kocuria varians, Nesterenkonia halobia, Nesterenkonia lacusekhoensis, Renibacterium salmoninarum, Rothia amarae, Rothia dentocariosa, Rothia mucilaginosa, Rothia nasimurium or Stomatococcus mucilaginosus; Mycobacteriaceae such as the genera Mycobacterium e.g. the species Mycobacterium africanum, Mycobacterium agri, Mycobacterium aichiense, Mycobacterium alvei, Mycobacterium asiaticum, Mycobacterium aurum, Mycobacterium austroafricanum, Mycobacterium 10 bohemicum, Mycobacterium botniense, Mycobacterium brumae, Mycobacterium chelonae subsp. abscessus, Mycobacterium chitae, Mycobacterium chlorophenolicum, Mycobacterium chubuense, Mycobacterium confluentis, Mycobacterium cookii, Mycobacterium diernhoferi, Mycobacterium doricum, Mycobacterium duvalii, Mycobacterium fallax, Mycobacterium farcinogenes, Mycobacterium flavescens, 15 Mycobacterium frederiksbergense, Mycobacterium gadium, Mycobacterium gilvum, Mycobacterium gordonae, Mycobacterium hassiacum, Mycobacterium hiberniae, Mycobacterium hodleri, Mycobacterium holsaticum, Mycobacterium komossense, Mycobacterium lacus, Mycobacterium madagascariense, Mycobacterium mageritense, Mycobacterium montefiorense, Mycobacterium moriokaense, Mycobacterium murale. 20 Mycobacterium neoaurum, Mycobacterium nonchromogenicum, Mycobacterium obuense, Mycobacterium palustre, Mycobacterium parafortuitum, Mycobacterium peregrinum, Mycobacterium phlei, Mycobacterium pinnipedii, Mycobacterium poriferae, Mycobacterium pulveris, Mycobacterium rhodesiae, Mycobacterium shottsii, 25 Mycobacterium sphagni, Mycobacterium terrae, Mycobacterium thermoresistibile, Mycobacterium tokaiense, Mycobacterium triviale, Mycobacterium tusciae or Mycobacterium vanbaalenii; Nocardiaceae such as the genera Nocardia, Rhodococcus e.g. the species Nocardia abscessus, Nocardia africana, Nocardia amarae, Nocardia asteroides, Nocardia autotrophica, Nocardia beijingensis, Nocardia brasiliensis, Nocardia brevicatena, Nocardia caishijiensis, Nocardia calcarea, Nocardia carnea, 30 Nocardia cellulans, Nocardia cerradoensis, Nocardia coeliaca, Nocardia corynebacterioides, Nocardia crassostreae, Nocardia cummidelens, Nocardia cyriacigeorgica, Nocardia farcinica, Nocardia flavorosea, Nocardia fluminea, Nocardia globerula, Nocardia hydrocarbonoxydans, Nocardia ignorata, Nocardia mediterranei, Nocardia nova, Nocardia orientalis, Nocardia otitidis-caviarum, Nocardia 35 otitidiscaviarum, Nocardia paucivorans, Nocardia petroleophila, Nocardia pinensis, Nocardia pseudobrasiliensis, Nocardia pseudovaccinii, Nocardia puris, Nocardia restricta, Nocardia rugosa, Nocardia salmonicida, Nocardia saturnea, Nocardia seriolae, Nocardia soli, Nocardia sulphurea, Nocardia transvalensis, Nocardia

uniformis, Nocardia vaccinii, Nocardia veterana or Nocardia vinacea;
 Pseudomonaceae such as the genera Azomonas, Azotobacter, Cellvibrio,
 Chryseomonas, Flaviomonas, Lampropedia, Mesophilobacter, Morococcus, Oligella,

43 Pseudomonas, Rhizobacter, Rugamonas, Serpens, Thermoleophilum, Xylophilus e.g. the species Azomonas agilis, Azomonas insignis, Azomonas macrocytogenes, Azotobacter agilis, Azotobacter agilis subsp. armeniae, Azotobacter armeniacus, Azotobacter beijerinckii, Azotobacter chroococcum, Azotobacter indicum, Azotobacter macrocytogenes, Azotobacter miscellum, Azotobacter nigricans subsp. nigricans, 5 Azotobacter paspali, Azotobacter salinestris, Azotobacter sp., Azotobacter vinelandii, Flavimonas oryzihabitans, Mesophilobacter marinus, Oligella urethralis, Pseudomonas acidovorans, Pseudomonas aeruginosa, Pseudomonas agarici, Pseudomonas alcaligenes, Pseudomonas aminovorans, Pseudomonas amygdali, Pseudomonas andropogonis, Pseudomonas anguilliseptica, Pseudomonas antarctica, Pseudomonas 10 antimicrobica, Pseudomonas antimycetica, Pseudomonas aptata, Pseudomonas arvilla, Pseudomonas asplenii, Pseudomonas atlantica, Pseudomonas atrofaciens, Pseudomonas aureofaciens, Pseudomonas avellanae, Pseudomonas azelaica, Pseudomonas azotocolligans; Pseudomonas balearica, Pseudomonas barkeri, Pseudomonas bathycetes, Pseudomonas beijerinckii, Pseudomonas brassicacearum, 15 Pseudomonas brenneri, Pseudomonas butanovora, Pseudomonas carboxydoflava, Pseudomonas carboxydohydrogena, Pseudomonas carboxydovorans, Pseudomonas carrageenovora, Pseudomonas caryophylli, Pseudomonas cepacia, Pseudomonas chloritidismutans, Pseudomonas chlororaphis, Pseudomonas cichorii, Pseudomonas citronellolis, Pseudomonas cocovenenans, Pseudomonas compransoris, 20 Pseudomonas congelans, Pseudomonas coronafaciens, Pseudomonas corrugata, Pseudomonas dacunhae, Pseudomonas delafieldii, Pseudomonas delphinii, Pseudomonas denitrificans, Pseudomonas desmolytica, Pseudomonas diminuta, Pseudomonas doudoroffii, Pseudomonas echinoides, Pseudomonas elongata, Pseudomonas extorquens, Pseudomonas extremorientalis, Pseudomonas facilis, 25 Pseudomonas ficuserectae, Pseudomonas flava, Pseudomonas flavescens, Pseudomonas fluorescens, Pseudomonas fragi, Pseudomonas frederiksbergensis, Pseudomonas fulgida, Pseudomonas fuscovaginae, Pseudomonas gazotropha, Pseudomonas gladioli, Pseudomonas glathei, Pseudomonas glumae, Pseudomonas graminis, Pseudomonas halophila, Pseudomonas helianthi, Pseudomonas huttiensis, 30 Pseudomonas hydrogenothermophila, Pseudomonas hydrogenovora, Pseudomonas indica, Pseudomonas indigofera, Pseudomonas iodinum, Pseudomonas kilonensis, Pseudomonas lachrymans, Pseudomonas lapsa, Pseudomonas lemoignei, Pseudomonas lemonnieri, Pseudomonas lundensis, Pseudomonas luteola, Pseudomonas maltophilia, Pseudomonas marginalis, Pseudomonas marginata, 35

Pseudomonas marina, Pseudomonas meliae, Pseudomonas mendocina,
Pseudomonas mesophilica, Pseudomonas mixta, Pseudomonas monteilii,
Pseudomonas morsprunorum, Pseudomonas multivorans, Pseudomonas natriegens,
Pseudomonas nautica, Pseudomonas nitroreducens, Pseudomonas oleovorans,
Pseudomonas oryzihabitans, Pseudomonas ovalis, Pseudomonas oxalaticus,

40 Pseudomonas oryzihabitans, Pseudomonas ovaiis, Pseudomonas oxaiaucus,
Pseudomonas palleronii, Pseudomonas paucimobilis, Pseudomonas phaseolicola,
Pseudomonas phenazinium, Pseudomonas pickettii, Pseudomonas pisi, Pseudomonas

plantarii, Pseudomonas plecoglossicida, Pseudomonas poae, Pseudomonas primulae, Pseudomonas proteolytica, Pseudomonas pseudoalcaligenes, Pseudomonas pseudoalcaligenes subsp. konjaci, Pseudomonas pseudoalcaligenes subsp. pseudoalcaligenes, Pseudomonas pseudoflava, Pseudomonas putida, Pseudomonas putida var. naraensis, Pseudomonas putrefaciens, Pseudomonas pyrrocinia, Pseudomonas radiora. Pseudomonas reptilivora, Pseudomonas rhodesiae, Pseudomonas rhodos, Pseudomonas riboflavina, Pseudomonas rubescens, Pseudomonas rubrisubalbicans, Pseudomonas ruhlandii, Pseudomonas saccharophila, Pseudomonas savastanoi, Pseudomonas savastanoi pvar. glycinea, Pseudomonas savastanoi pvar. phaseolicola, Pseudomonas solanacearum, Pseudomonas sp., 10 Pseudomonas spinosa, Pseudomonas stanieri, Pseudomonas stutzeri, Pseudomonas syringae, Pseudomonas syringae pvar. aptata, Pseudomonas syringae pvar. atrofaciens, Pseudomonas syringae pvar. coronafaciens, Pseudomonas syringae pvar. delphinii, Pseudomonas syringae pvar. glycinea, Pseudomonas syringae pvar. helianthi, Pseudomonas syringae pvar. lachrymans, Pseudomonas syringae pvar. 15 lapsa, Pseudomonas syringae pvar. morsprunorum, Pseudomonas syringae pvar. phaseolicola, Pseudomonas syringae pvar. primulae, Pseudomonas syringae pvar. syringae, Pseudomonas syringae pvar. tabaci, Pseudomonas syringae pvar. tomato, Pseudomonas syringae subsp. glycinea, Pseudomonas syringae subsp. savastanoi, Pseudomonas syringae subsp. syringae, Pseudomonas syzygii, Pseudomonas tabaci, 20 Pseudomonas taeniospiralis, Pseudomonas testosteroni, Pseudomonas thermocarboxydovorans, Pseudomonas thermotolerans, Pseudomonas thivervalensis, Pseudomonas tomato, Pseudomonas trivialis, Pseudomonas veronii, Pseudomonas vesicularis, Pseudomonas viridiflava, Pseudomonas viscogena, Pseudomonas woodsii, Rhizobacter dauci, Rhizobacter daucus or Xylophilus ampelinus; Rhizobiaceae such as 25 the genera Agrobacterium, Carbophilus, Chelatobacter, Ensifer, Rhizobium, Sinorhizobium e.g. the species Agrobacterium atlanticum, Agrobacterium ferrugineum, Agrobacterium gelatinovorum, Agrobacterium larrymoorei, Agrobacterium meteori. Agrobacterium radiobacter, Agrobacterium rhizogenes, Agrobacterium rubi, Agrobacterium stellulatum, Agrobacterium tumefaciens, Agrobacterium vitis, 30 Carbophilus carboxidus, Chelatobacter heintzii, Ensifer adhaerens, Ensifer arboris, Ensifer fredii, Ensifer kostiensis, Ensifer kummerowiae, Ensifer medicae, Ensifer meliloti, Ensifer saheli, Ensifer terangae, Ensifer xinjiangensis, Rhizobium ciceri Rhizobium etli, Rhizobium fredii, Rhizobium galegae, Rhizobium gallicum, Rhizobium giardinii. Rhizobium hainanense, Rhizobium huakuii, Rhizobium huautlense, Rhizobium 35 indigoferae, Rhizobium japonicum, Rhizobium leguminosarum, Rhizobium loessense,

Rhizobium loti, Rhizobium lupini, Rhizobium mediterraneum, Rhizobium meliloti, Rhizobium mongolense, Rhizobium phaseoli, Rhizobium radiobacter, Rhizobium rhizogenes, Rhizobium rubi, Rhizobium sullae, Rhizobium tianshanense, Rhizobium trifolii, Rhizobium tropici, Rhizobium undicola, Rhizobium vitis, Sinorhizobium 40 adhaerens, Sinorhizobium arboris, Sinorhizobium fredii, Sinorhizobium kostiense, Sinorhizobium kummerowiae, Sinorhizobium medicae, Sinorhizobium meliloti,

Sinorhizobium morelense, Sinorhizobium saheli or Sinorhizobium xinjiangense; Streptomycetaceae such as the genera Kitasatosprora, Streptomyces, Streptoverticillium e.g. the species Streptomyces abikoensis, Streptomyces aburaviensis, Streptomyces achromogenes subsp. achromogenes, Streptomyces achromogenes subsp. rubradiris, Streptomyces acidiscabies, Streptomyces acrimycini, 5 Streptomyces aculeolatus, Streptomyces afghaniensis, Streptomyces alanosinicus, Streptomyces albaduncus, Streptomyces albiaxialis, Streptomyces albidochromogenes, Streptomyces albidoflavus, Streptomyces albireticuli, Streptomyces albofaciens, Streptomyces alboflavus, Streptomyces albogriseolus, Streptomyces albolongus, Streptomyces alboniger, Streptomyces albospinus, 10 Streptomyces albosporeus subsp. albosporeus, Streptomyces albosporeus subsp. labilomyceticus, Streptomyces alboverticillatus, Streptomyces albovinaceus, Streptomyces alboviridis, Streptomyces albulus, Streptomyces albus subsp. albus, Streptomyces albus subsp. pathocidicus, Streptomyces almquistii, Streptomyces althioticus, Streptomyces amakusaensis, Streptomyces ambofaciens, Streptomyces 15 aminophilus, Streptomyces anandii, Streptomyces anthocyanicus, Streptomyces antibioticus, Streptomyces antimycoticus, Streptomyces anulatus, Streptomyces arabicus, Streptomyces ardus, Streptomyces arenae, Streptomyces argenteolus, Streptomyces armeniacus, Streptomyces asiaticus, Streptomyces asterosporus, Streptomyces atratus, Streptomyces atroaurantiacus, Streptomyces atroolivaceus, 20 Streptomyces atrovirens, Streptomyces aurantiacus, Streptomyces aurantiogriseus, Streptomyces aureocirculatus, Streptomyces aureofaciens, Streptomyces aureorectus, Streptomyces aureoversilis, Streptomyces aureoverticillatus, Streptomyces aureus, Streptomyces avellaneus, Streptomyces avermectinius, Streptomyces avermitilis, Streptomyces avidinii, Streptomyces azaticus, Streptomyces azureus, Streptomyces 25 baarnensis, Streptomyces bacillaris, Streptomyces badius, Streptomyces baldaccii, Streptomyces bambergiensis, Streptomyces beijiangensis, Streptomyces bellus, Streptomyces bikiniensis, Streptomyces biverticillatus, Streptomyces blastmyceticus, Streptomyces bluensis, Streptomyces bobili, Streptomyces bottropensis, Streptomyces brasiliensis, Streptomyces bungoensis, Streptomyces cacaoi subsp. asoensis, 30 Streptomyces cacaoi subsp. cacaoi, Streptomyces caelestis, Streptomyces caeruleus, Streptomyces californicus, Streptomyces calvus, Streptomyces canaries, Streptomyces candidus, Streptomyces canescens, Streptomyces cangkringensis, Streptomyces caniferus, Streptomyces canus, Streptomyces capillispiralis, Streptomyces capoamus, Streptomyces carpaticus, Streptomyces carpinensis, Streptomyces catenulae, 35 Streptomyces caviscables, Streptomyces cavourensis subsp. cavourensis, Streptomyces cavourensis subsp. washingtonensis, Streptomyces cellostaticus, Streptomyces celluloflavus, Streptomyces cellulolyticus, Streptomyces cellulosae, Streptomyces champavatii, Streptomyces chartreuses, Streptomyces chattanoogensis, Streptomyces chibaensis, Streptomyces chrestomyceticus, 40 Streptomyces chromofuscus, Streptomyces chryseus, Streptomyces chrysomallus subsp. chrysomallus, Streptomyces chrysomallus subsp. fumigatus, Streptomyces

46 cinereorectus, Streptomyces cinereoruber subsp. cinereoruber, Streptomyces cinereoruber subsp. fructofermentans, Streptomyces cinereospinus, Streptomyces cinereus, Streptomyces cinerochromogenes, Streptomyces cinnabarinus, Streptomyces cinnamonensis, Streptomyces cinnamoneus, Streptomyces cinnamoneus subsp. albosporus, Streptomyces cinnamoneus subsp. cinnamoneus, 5 Streptomyces cinnamoneus subsp. lanosus, Streptomyces cinnamoneus subsp. sparsus, Streptomyces cirratus, Streptomyces ciscaucasicus, Streptomyces citreofluorescens, Streptomyces clavifer, Streptomyces clavuligerus, Streptomyces cochleatus, Streptomyces coelescens, Streptomyces coelicoflavus, Streptomyces coelicolor. Streptomyces coeruleoflavus, Streptomyces coeruleofuscus, Streptomyces 10 coeruleoprunus, Streptomyces coeruleorubidus, Streptomyces coerulescens, Streptomyces collinus, Streptomyces colombiensis, Streptomyces corchorusii, Streptomyces costaricanus, Streptomyces cremeus, Streptomyces crystallinus, Streptomyces curacoi, Streptomyces cuspidosporus, Streptomyces cyaneofuscatus, Streptomyces cyaneus, Streptomyces cyanoalbus, Streptomyces cystargineus, 15 Streptomyces daghestanicus, Streptomyces diastaticus subsp. ardesiacus, Streptomyces diastaticus subsp. diastaticus, Streptomyces diastatochromogenes, Streptomyces distallicus, Streptomyces djakartensis, Streptomyces durhamensis, Streptomyces echinatus, Streptomyces echinoruber, Streptomyces ederensis, Streptomyces ehimensis, Streptomyces endus, Streptomyces enissocaesilis, 20 Streptomyces erumpens. Streptomyces erythraeus, Streptomyces erythrogriseus, Streptomyces eurocidicus, Streptomyces europaeiscabiei, Streptomyces eurythermus, Streptomyces exfoliates, Streptomyces felleus, Streptomyces fervens, Streptomyces fervens subsp. fervens, Streptomyces fervens subsp. melrosporus, Streptomyces filamentosus, Streptomyces filipinensis, Streptomyces fimbriatus, Streptomyces 25 fimicarius, Streptomyces finlayi, Streptomyces flaveolus, Streptomyces flaveus. Streptomyces flavidofuscus, Streptomyces flavidovirens, Streptomyces flaviscleroticus, Streptomyces flavofungini, Streptomyces flavofuscus, Streptomyces flavogriseus, Streptomyces flavopersicus, Streptomyces flavotricini, Streptomyces flavovariabilis, Streptomyces flavovirens, Streptomyces flavoviridis, Streptomyces flocculus, 30 Streptomyces floridae, Streptomyces fluorescens, Streptomyces fradiae, Streptomyces fragilis. Streptomyces fulvissimus, Streptomyces fulvorobeus, Streptomyces fumanus, Streptomyces fumigatiscleroticus, Streptomyces galbus, Streptomyces galilaeus, Streptomyces gancidicus, Streptomyces gardneri, Streptomyces gelaticus, Streptomyces geysiriensis, Streptomyces ghanaensis, Streptomyces gibsonii, 35 Streptomyces glaucescens, Streptomyces glaucosporus, Streptomyces glaucus, Streptomyces globisporus subsp. caucasicus, Streptomyces globisporus subsp.

Streptomyces glaucescens, Streptomyces glaucosporus, Streptomyces glaucus, Streptomyces globisporus subsp. caucasicus, Streptomyces globisporus subsp. flavofuscus, Streptomyces globisporus subsp. globisporus, Streptomyces globosus, Streptomyces glomeratus, Streptomyces glomeroaurantiacus, Streptomyces gobitricini, Streptomyces goshikiensis, Streptomyces gougerotii, Streptomyces graminearus, Streptomyces graminofaciens, Streptomyces griseinus, Streptomyces griseocameus, griseoaurantiacus, Streptomyces griseobrunneus, Streptomyces griseocameus,

WO 2005/014828 47 Streptomyces griseochromogenes, Streptomyces griseoflavus, Streptomyces griseofuscus, Streptomyces griseoincarnatus, Streptomyces griseoloalbus, Streptomyces griseolosporeus, Streptomyces griseolus, Streptomyces griseoluteus, Streptomyces griseomycini, Streptomyces griseoplanus, Streptomyces griseorubens, Streptomyces griseoruber, Streptomyces griseorubiginosus, Streptomyces griseosporeus, Streptomyces griseostramineus, Streptomyces griseoverticillatus, Streptomyces griseoviridis, Streptomyces griseus subsp. alpha, Streptomyces griseus subsp. cretosus, Streptomyces griseus subsp. griseus, Streptomyces griseus subsp. solvifaciens, Streptomyces hachijoensis, Streptomyces halstedii, Streptomyces hawaiiensis, Streptomyces heliomycini, Streptomyces helvaticus, Streptomyces herbaricolor, Streptomyces hiroshimensis, Streptomyces hirsutus, Streptomyces humidus, Streptomyces humiferus, Streptomyces hydrogenans, Streptomyces hygroscopicus subsp. angustmyceticus, Streptomyces hygroscopicus subsp. decoyicus, Streptomyces hygroscopicus subsp. glebosus, Streptomyces hygroscopicus subsp. hygroscopicus, Streptomyces hygroscopicus subsp. ossamyceticus, Streptomyces iakyrus, Streptomyces indiaensis, Streptomyces indigoferus, Streptomyces indonesiensis, Streptomyces intermedius, Streptomyces inusitatus, Streptomyces ipomoeae, Streptomyces janthinus, Streptomyces javensis, Streptomyces kanamyceticus, Streptomyces kashmirensis, Streptomyces kasugaensis, Streptomyces katrae, Streptomyces kentuckensis, Streptomyces kifunensis, Streptomyces kishiwadensis, Streptomyces kunmingensis, Streptomyces kurssanovii, Streptomyces labedae, Streptomyces laceyi, Streptomyces ladakanum, Streptomyces lanatus, Streptomyces lateritius, Streptomyces laurentii, Streptomyces lavendofoliae, Streptomyces lavendulae subsp. grasserius, Streptomyces lavendulae subsp. lavendulae, Streptomyces lavenduligriseus, Streptomyces lavendulocolor, Streptomyces levis, Streptomyces libani subsp. libani, Streptomyces libani subsp. rufus, Streptomyces lienomycini, Streptomyces lilacinus, Streptomyces limosus, Streptomyces lincolnensis, Streptomyces lipmanii, Streptomyces litmocidini, Streptomyces Iomondensis, Streptomyces Iongisporoflavus, Streptomyces longispororuber, Streptomyces longisporus, Streptomyces longwoodensis, Streptomyces lucensis, Streptomyces luridiscabiei, Streptomyces luridus, Streptomyces lusitanus, Streptomyces luteireticuli, Streptomyces luteogriseus, Streptomyces luteosporeus, Streptomyces luteoverticillatus, Streptomyces lydicus, Streptomyces macrosporus, Streptomyces malachitofuscus, Streptomyces malachitospinus, Streptomyces malaysiensis, Streptomyces mashuensis, Streptomyces massasporeus, Streptomyces matensis, Streptomyces mauvecolor, Streptomyces mediocidicus, Streptomyces mediolani, Streptomyces megasporus,

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35 Streptomyces melanogenes, Streptomyces melanosporofaciens, Streptomyces mexicanus, Streptomyces michiganensis, Streptomyces microflavus, Streptomyces minutiscleroticus, Streptomyces mirabilis, Streptomyces misakiensis, Streptomyces 40 misionensis, Streptomyces mobaraensis, Streptomyces monomycini, Streptomyces morookaensis, Streptomyces murinus, Streptomyces mutabilis, Streptomyces

mutomycini, Streptomyces naganishii, Streptomyces narbonensis, Streptomyces nashvillensis. Streptomyces netropsis, Streptomyces neyagawaensis, Streptomyces niger, Streptomyces nigrescens, Streptomyces nigrifaciens, Streptomyces nitrosporeus, Streptomyces niveiciscabiei, Streptomyces niveoruber, Streptomyces niveus, Streptomyces noboritoensis, Streptomyces nodosus, Streptomyces nogalater, 5 Streptomyces noiiriensis, Streptomyces noursei, Streptomyces novaecaesareae, Streptomyces ochraceiscleroticus, Streptomyces odorifer, Streptomyces olivaceiscleroticus, Streptomyces olivaceoviridis, Streptomyces olivaceus, Streptomyces olivochromogenes, Streptomyces olivomycini, Streptomyces olivoreticuli. Streptomyces olivoreticuli subsp. cellulophilus, Streptomyces olivoreticuli subsp. 10 olivoreticuli, Streptomyces olivoverticillatus, Streptomyces olivoviridis, Streptomyces omivaensis. Streptomyces orinoci, Streptomyces pactum, Streptomyces paracochleatus, Streptomyces paradoxus, Streptomyces parvisporogenes, Streptomyces parvulus, Streptomyces parvus, Streptomyces peucetius, Streptomyces phaeochromogenes, Streptomyces phaeofaciens, Streptomyces phaeopurpureus, 15 Streptomyces phaeoviridis, Streptomyces phosalacineus, Streptomyces pilosus, Streptomyces platensis, Streptomyces plicatus, Streptomyces pluricolorescens, Streptomyces polychromogenes, Streptomyces poonensis, Streptomyces praecox, Streptomyces prasinopilosus, Streptomyces prasinosporus, Streptomyces prasinus, Streptomyces prunicolor, Streptomyces psammoticus, Streptomyces 20 pseudoechinosporeus, Streptomyces pseudogriseolus, Streptomyces pseudovenezuelae, Streptomyces pulveraceus, Streptomyces puniceus, Streptomyces puniciscabiei, Streptomyces purpeofuscus, Streptomyces purpurascens, Streptomyces purpureus, Streptomyces purpurogeneiscleroticus, Streptomyces racemochromogenes, Streptomyces rameus, Streptomyces ramulosus, Streptomyces 25 rangoonensis, Streptomyces recifensis, Streptomyces rectiverticillatus, Streptomyces rectiviolaceus, Streptomyces regensis, Streptomyces resistomycificus, Streptomyces reticuliscabiei, Streptomyces rhizosphaericus, Streptomyces rimosus subsp. paromomycinus, Streptomyces rimosus subsp. rimosus, Streptomyces rishiriensis, Streptomyces rochei, Streptomyces roseiscleroticus, Streptomyces roseodiastaticus, 30 Streptomyces roseoflavus, Streptomyces roseofulvus, Streptomyces roseolilacinus, Streptomyces roseolus, Streptomyces roseosporus, Streptomyces roseoverticillatus, Streptomyces roseoviolaceus, Streptomyces roseoviridis, Streptomyces rubber, Streptomyces rubiginosohelvolus, Streptomyces rubiginosus, Streptomyces rubrogriseus, Streptomyces rutgersensis subsp. castelarensis, Streptomyces 35 rutgersensis subsp. rutgersensis, Streptomyces salmonis, Streptomyces sampsonii, Streptomyces sanglieri, Streptomyces sannanensis, Streptomyces sapporonensis. Streptomyces scabiei, Streptomyces sclerotialus, Streptomyces scopiformis, Streptomyces seoulensis, Streptomyces septatus, Streptomyces setae, Streptomyces setonii, Streptomyces showdoensis, Streptomyces sindenensis, Streptomyces 40

sioyaensis, Streptomyces somaliensis, Streptomyces sparsogenes, Streptomyces spectabilis. Streptomyces speibonae. Streptomyces speleomycini, Streptomyces

spheroids, Streptomyces spinoverrucosus, Streptomyces spiralis, Streptomyces spiroverticillatus, Streptomyces spitsbergensis, Streptomyces sporocinereus, Streptomyces sporoclivatus, Streptomyces spororaveus, Streptomyces sporoverrucosus, Streptomyces stelliscabiei, Streptomyces stramineus, Streptomyces subrutilus, Streptomyces sulfonofaciens, Streptomyces sulphurous, Streptomyces 5 syringium, Streptomyces tanashiensis, Streptomyces tauricus, Streptomyces tendae, Streptomyces termitum, Streptomyces thermoalcalitolerans, Streptomyces thermoautotrophicus, Streptomyces thermocarboxydovorans, Streptomyces thermocarboxydus, Streptomyces thermocoprophilus, Streptomyces thermodiastaticus, Streptomyces thermogriseus, Streptomyces thermolineatus, Streptomyces 10 thermonitrificans, Streptomyces thermospinosisporus, Streptomyces thermoviolaceus subsp. apingens, Streptomyces thermoviolaceus subsp. thermoviolaceus, Streptomyces thermovulgaris, Streptomyces thioluteus, Streptomyces torulosus, Streptomyces toxytricini, Streptomyces tricolor, Streptomyces tubercidicus, Streptomyces tuirus, Streptomyces turgidiscabies, Streptomyces umbrinus, 15 Streptomyces variabilis, Streptomyces variegates, Streptomyces varsoviensis, Streptomyces vastus, Streptomyces venezuelae, Streptomyces vinaceus, Streptomyces vinaceusdrappus, Streptomyces violaceochromogenes, Streptomyces violaceolatus, Streptomyces violaceorectus, Streptomyces violaceoruber, Streptomyces violaceorubidus, Streptomyces violaceus, Streptomyces violaceusniger, Streptomyces 20 violarus, Streptomyces violascens, Streptomyces violatus, Streptomyces violens, Streptomyces virens, Streptomyces virginiae, Streptomyces viridiflavus, Streptomyces viridiviolaceus, Streptomyces viridobrunneus, Streptomyces viridochromogenes, Streptomyces viridodiastaticus, Streptomyces viridosporus, Streptomyces vitaminophileus, Streptomyces vitaminophilus, Streptomyces wedmorensis, 25 Streptomyces werraensis, Streptomyces willmorei, Streptomyces xanthochromogenes, Streptomyces xanthocidicus, Streptomyces xantholiticus, Streptomyces xanthophaeus, Streptomyces yatensis, Streptomyces yerevanensis, Streptomyces yogyakartensis, Streptomyces yokosukanensis, Streptomyces yunnanensis, Streptomyces zaomyceticus, Streptoverticillium abikoense, Streptoverticillium albireticuli, 30 Streptoverticillium alboverticillatum, Streptoverticillium album, Streptoverticillium ardum, Streptoverticillium aureoversale, Streptoverticillium aureoversile, Streptoverticillium baldaccii , Streptoverticillium biverticillatum, Streptoverticillium blastmyceticum, Streptoverticillium cinnamoneum subsp. albosporum, Streptomyces cinnamoneus subsp. albosporus, Streptoverticillium cinnamoneum subsp. cinnamoneum, 35 Streptoverticillium cinnamoneum subsp. lanosum, Streptoverticillium cinnamoneum subsp. sparsum, Streptoverticillium distallicum, Streptoverticillium ehimense, Streptoverticillium eurocidicum, Streptoverticillium fervens subsp. fervens, Streptoverticillium fervens subsp. melrosporus, Streptoverticillium flavopersicum,

40 Streptoverticillium griseocarneum, Streptoverticillium griseoverticillatum, Streptoverticillium hachijoense, Streptoverticillium hiroshimense, Streptoverticillium kashmirense, Streptoverticillium kentuckense, Streptoverticillium kishiwadense,

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Streptoverticillium ladakanum, Streptoverticillium lavenduligriseum, Streptoverticillium lilacinum, Streptoverticillium luteoverticillatum, Streptoverticillium mashuense, Streptoverticillium mobaraense, Streptoverticillium morookaense, Streptoverticillium netropsis, Streptoverticillium olivomycini, Streptomyces olivomycini, Streptoverticillium olivoreticuli subsp. cellulophilum, Streptoverticillium olivoreticuli subsp. olivoreticuli, Streptoverticillium olivoreticulum, Streptoverticillium olivoreticulum subsp. cellulophilum, Streptoverticillium olivoverticillatum, Streptoverticillium orinoci, Streptoverticillium parvisporogenes, Streptoverticillium parvisporogenum, Streptoverticillium rectiverticillatum, Streptoverticillium reticulum subsp. protomycicum, Streptoverticillium roseoverticillatum, Streptoverticillium salmonis, Streptoverticillium sapporonense, Streptoverticillium septatum, Streptoverticillium syringium, Streptoverticillium thioluteum, Streptoverticillium verticillium subsp. quantum, Streptoverticillium verticillium viridoflavum.

Particular preferred strains are strains selected from the group [0092.0.0.0] consisting of Bacillaceae, Brevibacteriaceae, Corynebacteriaceae, Nocardiaceae, 15 Mycobacteriaceae, Streptomycetaceae, Enterobacteriaceae such as Bacillus circulans, Bacillus subtilis, Bacillus sp., Brevibacterium albidum, Brevibacterium album, Brevibacterium cerinum, Brevibacterium flavum, Brevibacterium glutamigenes, Brevibacterium iodinum, Brevibacterium ketoglutamicum, Brevibacterium lactofermentum, Brevibacterium linens, Brevibacterium roseum, Brevibacterium 20 saccharolyticum, Brevibacterium sp., Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium ammoniagenes, Corynebacterium glutamicum (= Micrococcus glutamicum), Corynebacterium melassecola, Corynebacterium sp., Nocardia rhodochrous (Rhodococcus rhodochrous). Mycobacterium rhodochrous, Streptomyces lividans and Escherichia coli 25 especially Escherichia coli K12.

[0093.0.0.0] In addition particular preferred strains are strains selected from the group consisting of Cryptococcaceae, Saccharomycetaceae, Schizosaccharomycetacease such as the genera Candida, Hansenula, Pichia, Saccharomyces and Schizosaccharomyces preferred are strains selected from the group consisting of the species Rhodotorula rubra, Rhodotorula glutinis, Rhodotorula graminis, Yarrowia lipolytica, Sporobolomyces salmonicolor, Sporobolomyces shibatanus, Saccharomyces cerevisiae, Candida boidinii, Candida bombicola, Candida cylindracea, Candida parapsilosis, Candida rugosa, Candida tropicalis, Pichia methanolica and Pichia pastoris especially Saccharomyces cerevisiae.

[0094.0.0.0] Anacardiaceae such as the genera Pistacia, Mangifera, Anacardium e.g. the species *Pistacia vera* [pistachios, Pistazie], *Mangifer indica* [Mango] or *Anacardium occidentale* [Cashew]; Asteraceae such as the genera Calendula, Carthamus, Centaurea, Cichorium, Cynara, Helianthus, Lactuca, Locusta, Tagetes, Valeriana e.g. the species *Calendula officinalis* [Marigold], *Carthamus tinctorius* [safflower],

51 Centaurea cyanus [cornflower], Cichorium intybus [blue daisy], Cynara scolymus [Artichoke], Helianthus annus [sunflower], Lactuca sativa, Lactuca crispa, Lactuca esculenta, Lactuca scariola L. ssp. sativa, Lactuca scariola L. var. integrata, Lactuca scariola L. var. integrifolia, Lactuca sativa subsp. romana, Locusta communis, Valeriana locusta [lettuce], Tagetes lucida, Tagetes erecta or Tagetes tenuifolia 5 [Marigold]; Apiaceae such as the genera Daucus e.g. the species Daucus carota [carrot]; Betulaceae such as the genera Corylus e.g. the species Corylus avellana or Corylus colurna [hazelnut]; Boraginaceae such as the genera Borago e.g. the species Borago officinalis [borage]; Brassicaceae such as the genera Brassica, Melanosinapis, Sinapis, Arabadopsis e.g. the species Brassica napus, Brassica rapa ssp. [canola, 10 oilseed rape, turnip rape], Sinapis arvensis Brassica juncea, Brassica juncea var. juncea, Brassica juncea var. crispifolia, Brassica juncea var. foliosa, Brassica nigra, Brassica sinapioides, Melanosinapis communis [mustard], Brassica oleracea [fodder beet] or Arabidopsis thaliana; Bromeliaceae such as the genera Anana, Bromelia e.g. the species Anana comosus, Ananas ananas or Bromelia comosa [pineapple]; 15 Caricaceae such as the genera Carica e.g. the species Carica papaya [papaya]; Cannabaceae such as the genera Cannabis e.g. the species Cannabis sative [hemp], Convolvulaceae such as the genera Ipomea, Convolvulus e.g. the species Ipomoea batatus, Ipomoea pandurata, Convolvulus batatas, Convolvulus tiliaceus, Ipomoea fastigiata, Ipomoea tiliacea, Ipomoea triloba or Convolvulus panduratus [sweet potato, 20 Man of the Earth, wild potato], Chenopodiaceae such as the genera Beta, i.e. the species Beta vulgaris, Beta vulgaris var. altissima, Beta vulgaris var. Vulgaris, Beta maritima, Beta vulgaris var. perennis, Beta vulgaris var. conditiva or Beta vulgaris var. esculenta [sugar beet]; Cucurbitaceae such as the genera Cucubita e.g. the species Cucurbita maxima, Cucurbita mixta, Cucurbita pepo or Cucurbita moschata [pumpkin, 25 squash]; Elaeagnaceae such as the genera Elaeagnus e.g. the species Olea europaea [olive]; Ericaceae such as the genera Kalmia e.g. the species Kalmia latifolia, Kalmia angustifolia, Kalmia microphylla, Kalmia polifolia, Kalmia occidentalis, Cistus chamaerhodendros or Kalmia lucida [American laurel, broad-leafed laurel, calico bush, spoon wood, sheep laurel, alpine laurel, bog laurel, western bog-laurel, swamp-laurel]; 30 Euphorbiaceae such as the genera Manihot, Janipha, Jatropha, Ricinus e.g. the species Manihot utilissima, Janipha manihot,, Jatropha manihot., Manihot aipil, Manihot dulcis, Manihot manihot, Manihot melanobasis, Manihot esculenta [manihot, arrowroot, tapioca, cassava] or Ricinus communis [castor bean, Castor Oil Bush, Castor Oil Plant, Palma Christi, Wonder Tree]; Fabaceae such as the genera Pisum, Albizia, 35 Cathormion, Feuillea, Inga, Pithecolobium, Acacia, Mimosa, Medicajo, Glycine, Dólichos, Phaseolus, Soja e.g. the species Pisum sativum, Pisum arvense, Pisum humile [pea], Albizia berteriana, Albizia julibrissin, Albizia lebbeck, Acacia berteriana, Acacia littoralis, Albizia berteriana, Albizzia berteriana, Cathormion berteriana, Feuillea berteriana, Inga fragrans, Pithecellobium berterianum, Pithecellobium fragrans,

Pithecolobium berterianum, Pseudalbizzia berteriana, Acacia julibrissin, Acacia nemu, Albizia nemu, Feuilleea julibrissin, Mimosa julibrissin, Mimosa speciosa, Sericanrda

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julibrissin, Acacia lebbeck, Acacia macrophylla, Albizia lebbek, Feuilleea lebbeck, Mimosa lebbeck, Mimosa speciosa [bastard logwood, silk tree, East Indian Walnut], Medicago sativa, Medicago falcata, Medicago varia [alfalfa] Glycine max Dolichos soja, Glycine gracilis, Glycine hispida, Phaseolus max, Soja hispida or Soja max [soybean]; Geraniaceae such as the genera Pelargonium, Cocos, Oleum e.g. the species Cocos nucifera, Pelargonium grossularioides or Oleum cocois [coconut]; Gramineae such as the genera Saccharum e.g. the species Saccharum officinarum; Juglandaceae such as the genera Juglans, Wallia e.g. the species Juglans regia, Juglans ailanthifolia, Juglans sieboldiana, Juglans cinerea, Wallia cinerea, Juglans bixbyi, Juglans californica, Juglans hindsii, Juglans intermedia, Juglans jamaicensis, Juglans major, Juglans microcarpa, Juglans nigra or Wallia nigra [walnut, black walnut, common walnut, persian walnut, white walnut, butternut, black walnut]; Lauraceae such as the genera Persea, Laurus e.g. the species laurel Laurus nobilis [bay, laurel, bay laurel, sweet] bay], Persea americana Persea americana, Persea gratissima or Persea persea [avocado]; Leguminosae such as the genera Arachis e.g. the species Arachis hypogaea [peanut]; Linaceae such as the genera Linum, Adenolinum e.g. the species Linum usitatissimum, Linum humile, Linum austriacum, Linum bienne, Linum angustifolium, Linum catharticum, Linum flavum, Linum grandiflorum, Adenolinum grandiflorum, Linum lewisii, Linum narbonense, Linum perenne, Linum perenne var. lewisii, Linum pratense or Linum trigynum [flax, linseed]; Lythrarieae such as the genera Punica e.g. the species Punica granatum [pomegranate]; Malvaceae such as the genera Gossypium e.g. the species Gossypium hirsutum, Gossypium arboreum, Gossypium barbadense, Gossypium herbaceum or Gossypium thurberi [cotton]; Musaceae such as the genera Musa e.g. the species Musa nana, Musa acuminata, Musa paradisiaca, Musa spp. [banana]; Onagraceae such as the genera Camissonia, Oenothera e.g. the species Oenothera biennis or Camissonia brevipes [primrose, evening primrosel; Palmae such as the genera Elacis e.g. the species Elaeis guineensis [oil plam]; Papaveraceae such as the genera Papaver e.g. the species Papaver orientale, Papaver rhoeas, Papaver dubium [poppy, oriental poppy, corn poppy, field poppy, shirley poppies, field poppy, long-headed poppy, long-pod poppy]; Pedaliaceae such as the genera Sesamum e.g. the species Sesamum indicum [sesame]; Piperaceae such as the genera Piper, Artanthe, Peperomia, Steffensia e.g. the species Piper aduncum, Piper amalago, Piper angustifolium, Piper auritum, Piper betel, Piper cubeba, Piper longum, Piper nigrum, Piper retrofractum, Artanthe adunca, Artanthe elongata, Peperomia elongata, Piper elongatum, Steffensia elongata. [Cayenne pepper, wild pepper]; Poaceae such as the genera Hordeum, Secale, Avena, Sorghum, Andropogon, Holcus, Panicum, Oryza, Zea, Triticum e.g. the species Hordeum vulgare, Hordeum jubatum, Hordeum murinum, Hordeum secalinum, Hordeum distiction Hordeum aegiceras, Hordeum hexastiction., Hordeum hexastichum, Hordeum irregulare, Hordeum sativum, Hordeum secalinum [barley, pearl barley, foxtail barley, wall barley, meadow barley], Secale cereale [rye], Avena

sativa, Avena fatua, Avena byzantina, Avena fatua var. sativa, Avena hybrida [oat],

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**53** Sorghum bicolor, Sorghum halepense, Sorghum saccharatum, Sorghum vulgare, Andropogon drummondii, Holcus bicolor, Holcus sorghum, Sorghum aethiopicum, Sorghum arundinaceum, Sorghum caffrorum, Sorghum cernuum, Sorghum dochna, Sorghum drummondii, Sorghum durra, Sorghum guineense, Sorghum lanceolatum, Sorghum nervosum, Sorghum saccharatum, Sorghum subglabrescens, Sorghum 5 verticilliflorum, Sorghum vulgare, Holcus halepensis, Sorghum miliaceum millet, Panicum militaceum [Sorghum, millet], Oryza sativa, Oryza latifolia [rice], Zea mays [corn, maize] Triticum aestivum, Triticum durum, Triticum turgidum, Triticum hybernum, Triticum macha, Triticum sativum or Triticum vulgare [wheat, bread wheat, common wheat], Proteaceae such as the genera Macadamia e.g. the species Macadamia intergrifolia [macadamia]; Rubiaceae such as the genera Coffea e.g. the species Cofea spp., Coffea arabica, Coffea canephora or Coffea liberica [coffee]; Scrophulariaceae such as the genera Verbascum e.g. the species Verbascum blattaria, Verbascum chaixii, Verbascum densiflorum, Verbascum lagurus, Verbascum longifolium, Verbascum lychnitis, Verbascum nigrum, Verbascum olympicum, Verbascum 15 phlomoides, Verbascum phoenicum, Verbascum pulverulentum or Verbascum thapsus [mullein, white moth mullein, nettle-leaved mullein, dense-flowered mullein, silver mullein, long-leaved mullein, white mullein, dark mullein, greek mullein, orange mullein, purple mullein, hoary mullein, great mullein]; Solanaceae such as the genera Capsicum, Nicotiana, Solanum, Lycopersicon e.g. the species Capsicum annuum, 20 Capsicum annuum var. glabriusculum, Capsicum frutescens [pepper], Capsicum annuum [paprika], Nicotiana tabacum, Nicotiana alata, Nicotiana attenuata, Nicotiana glauca, Nicotiana langsdorffii, Nicotiana obtusifolia, Nicotiana quadrivalvis, Nicotiana repanda, Nicotiana rustica, Nicotiana sylvestris [tobacco], Solanum tuberosum [potato],

25 Solanum melongena [egg-plant] (Lycopersicon esculentum, Lycopersicon lycopersicum., Lycopersicon pyriforme, Solanum integrifolium or Solanum lycopersicum [tomato]; Sterculiaceae such as the genera Theobroma e.g. the species Theobroma cacao [cacao]; Theaceae such as the genera Camellia e.g. the species Camellia sinensis) [tea].

30 All abovementioned organisms can in princible also function as host organisms.

[0095.0.0.0] Particular preferred plants are plants selected from the group consisting of Asteraceae such as the genera Helianthus, Tagetes e.g. the species Helianthus annus [sunflower], Tagetes lucida, Tagetes erecta or Tagetes tenuifolia [Marigold]; Brassicaceae such as the genera Brassica, Arabadopsis e.g. the species Brassica napus, Brassica rapa ssp., Brassica juncea [canola, oilseed rape, turnip rape] or Arabidopsis thaliana; Fabaceae such as the genera Glycine e.g. the species Glycine max, Soja hispida or Soja max [soybean]; Linaceae such as the genera Linum e.g. the species Linum usitatissimum, [flax, linseed]; Poaceae such as the genera Hordeum, Secale, Avena, Sorghum, Oryza, Zea, Triticum e.g. the species Hordeum vulgare [barley]; Secale cereale [rye], Avena sativa, Avena fatua, Avena byzantina, Avena fatua var. sativa, Avena hybrida [oat], Sorghum bicolor [Sorghum, millet], Oryza sativa,

Oryza latifolia [rice], Zea mays [corn, maize] Triticum aestivum, Triticum durum, Triticum turgidum, Triticum hybernum, Triticum macha, Triticum sativum or Triticum vulgare [wheat, bread wheat, common wheat]; Solanaceae such as the genera Solanum, Lycopersicon e.g. the species Solanum tuberosum [potato], Lycopersicon esculentum, Lycopersicon lycopersicum., Lycopersicon pyriforme, Solanum integrifolium or Solanum lycopersicum [tomato].

[0096.0.0.0] All abovementioned organisms can in princible also function as host organisms.

[0097.0.0.0] With regard to the nucleic acid sequence as depicted below a nucleic acid construct which contains a nucleic acid sequence mentioned herein or an organism (= transgenic organism) which is transformed with said nucleic acid sequence or said nucleic acid construct, "transgene" means all those constructs which have been brought about by genetic manipulation methods, preferably in which either

- the nucleic acid sequence as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, a) 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 15 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 20 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 or 25 a derivative thereof, or
- b) a genetic regulatory element, for example a promoter, which is functionally linked to the nucleic acid sequence as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361,

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363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 or a derivative thereof, or

## c) (a) and (b)

is/are not present in its/their natural genetic environment or has/have been modified by means of genetic manipulation methods, it being possible for the modification to be, by way of example, a substitution, addition, deletion, inversion or insertion of one or more nucleotide. "Natural genetic environment" means the natural chromosomal locus in the organism of origin or the presence in a genomic library. In the case of a genomic library, the natural, genetic environment of the nucleic acid sequence is preferably at least partially still preserved. The environment flanks the nucleic acid sequence at least on one side and has a sequence length of at least 50 bp, preferably at least 500 bp, particularly preferably at least 1000 bp, very particularly preferably at least 5000 bp.

[0098.0.0.0] The use of the nucleic acid sequence according to the invention or of the nucleic acid construct according to the invention for the generation of transgenic plants is therefore also subject matter of the invention.

**[0099.0.0.0]** The fine chemical, which is synthesized in the organism, in particular the microorganism, the cell, the tissue or the plant, of the invention can be isolated if desired. Depending on the use of the fine chemical, different purities resulting from the purification may be advantageous as will be described herein below.

[0100.0.0.0] In an advantageous embodiment of the invention, the organism takes the form of a plant whose fine chemical content is modified advantageously owing to the nucleic acid molecule of the present invention expressed. This is important for plant breeders since, for example, the nutritional value of organisms such as a plant is very often limited by its amino acid, protein, co-factor and/or vitamin content to mention only a couple of them. For example in feed for monogastric animals a few essential amino acids such as lysine, threonine or methionine are very often limiting. After the biological activity of the nucleic acid and/or protein of the invention has been increased or generated, or after the expression of nucleic acid molecule or polypeptide according to the invention has been generated or increased, the transgenic plant generated thus is grown on or in a nutrient medium or else in the soil and subsequently harvested.

**[0101.0.0.0]** The plants or parts thereof, e.g. the leaves, roots, flowers, and/or stems and/or other harvestable material as described below, can then be used directly as foodstuffs or animal feeds or else be further processed. Again, the amino acids can be purified further in the customary manner via extraction and precipitation or via ion exchangers and other methods known to the person skilled in the art and described herein below. Products which are suitable for various applications and which result from these different processing procedures are for example amino acids or amino acid compositions which can still comprise further plant components in different amounts,

advantageously in the range of from 0 to 99% by weight or more, preferably from below 90%, 80%, 70%, 60% or 50% by weight, especially preferably below 40%, 30%, 20% or 10% by weight. The plants can also advantageously be used directly without further processing, e.g. as feed or for extraction.

- [0102.0.0.0] The chemically pure fine chemical or chemically pure compositions comprising the fine chemical may also be produced by the process described above. To this end, the fine chemical or the compositions are isolated in the known manner from an organism according to the invention, such as the microorganisms, non-human animal or the plants, and/or their culture medium in which or on which the organisms had been grown. These chemically pure fine chemical or said compositions are advantageous for applications in the field of the food industry, the cosmetics industry or the pharmaceutical industry.
  - **[0103.0.0.0]** Thus, the content of plant components and preferably also further impurities is as low as possible, and the abovementioned fine chemical are obtained in as pure form as possible. In these applications, the content of plant components advantageously amounts to less than 10% by weight, preferably 1% by weight, more preferably 0.1% by weight, very especially preferably 0.01% by weight or less.

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- [0104.0.0.0] Accordingly, the fine chemical produced by the present invention is at least 0,1% by weight pure, preferably more than 1% by weight pure, more preferred 10% by weight pure, even more preferred are more than 50%, 60%, 70% or 80% by weight pure, even more preferred are more than 90%, 91%, 92%, 93%, 94% or 95% weight pure, most preferred are 96%, 97%, 98% or 99% by weight or more pure.
- [0105.0.0.0] In this context, the amount of the fine chemical in a cell of the invention may be increased according to the process of the invention by at least a factor of 1.1, preferably at least a factor of 1.5; 2; or 5, especially preferably by at least a factor of 10 or 30, very especially preferably by at least a factor of 50, in comparison with the wild type, control or reference. Preferrably, said increase is found in a tissue of an organism, more preferred in the organism itself or in a harvestable part thereof.
- [0106.0.0.0] In principle, the fine chemicals produced can be increased in two ways by the process according to the invention. The pool of free fine chemicals, in particular of the free fine chemical, and/or the content of bound for example protein-bound fine chemicals, in particular of the protein-bound fine chemical may advantageously be increased.
- [0107.0.0.0] It may be advantageous to increase the pool of free fine chemical in the transgenic organisms by the process according to the invention in order to isolate high amounts of the pure fine chemical.

[0108.0.0.0] In another preferred embodiment of the invention a combination of the increased expression of the nucleic acid sequence or the protein of the invention together with the transformation of a protein or polypeptid, which functions as a sink for the desired fine chemical such as an amino acid for example methionine, lysine or threonine in the organism is useful to increase the production of the fine chemical (see US 5,589,616, WO 96/38574, WO 97/07665, WO 97/28247, US 4,886,878, US 5,082,993 and US 5,670,635). Galili et al. [Transgenic Res. 2000] showed, that enhancing the synthesis of threonine by a feed back insensitive aspertate kinase didnot lead only to in increase in free threonine but also in protein bound threonine.

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10 [0109.0.0.0] In may also be advantageous to increase the content of the bound fine . . . . . chemical.

[0110.0.0.0] In a preferred embodiment, the fine chemical is produced in accordance with the invention and, if desired, is isolated. The production of further fine chemicals for example amino acids such as lysine and of amino acid mixtures by the process according to the invention is advantageous.

[0111.0.0.0] In the case of the fermentation of microorganisms, the abovementioned fine chemical e.g. amino acid or mixtures of amino acids may accumulate in the medium and/or the cells. If microorganisms are used in the process according to the invention, the fermentation broth can be processed after the cultivation. Depending on the requirement, all or some of the biomass can be removed from the fermentation broth by separation methods such as, for example, centrifugation, filtration, decanting or a combination of these methods, or else the biomass can be left in the fermentation broth. The fermentation broth can subsequently be reduced, or concentrated, with the aid of known methods such as, for example, rotary evaporator, thin-layer evaporator, falling film evaporator, by reverse osmosis or by nanofiltration. This concentrated fermentation broth can subsequently be processed by lyophilization, spray drying, spray granulation or by other methods.

[0112.0.0.0] To purify a fine chemical such as an amino acid, a product-containing fermentation broth from which the biomass has been separated may be subjected to chromatography with a suitable resin such as ion exchange resin for example anion or cation exchange resin, hydrophobic resin or hydrophilic resin for example epoxy resin, polyurethane resin or polyacrylamid resin, or resin for separation according to the molecular weight of the compounds for example polyvinyl chloride homopolymer resin or resins composed for example of polymers of acrylic acid, crosslinked with polyalkenyl ethers or divinyl glycol such as Carbopol®, Pemulen® and Noveon®. If necessary these chromatography steps may be repeated using the same or other chromatography resins. The skilled worker is familiar with the choice of suitable chromatography resins and their most effective use. The purified product may be

concentrated by filtration or ultrafiltration and stored at a temperature, which ensures the maximum stability of the product.

[0113.0.0.0] The identity and purity of the compound(s) isolated can be determined by prior-art techniques. They encompass high-performance liquid chromatography (HPLC), spectroscopic methods, mass spectrometry (MS), staining methods, thin-layer chromatography, NIRS, enzyme assays or microbiological assays. These analytical methods are compiled in: Patek et al. (1994) Appl. Environ. Microbiol. 60:133-140; Malakhova et al. (1996) Biotekhnologiya 11 27-32; and Schmidt et al. (1998)
Bioprocess Engineer. 19:67-70. Ulmann's Encyclopedia of Industrial Chemistry (1996) Bd. A27, VCH Weinheim, pp. 89-90, pp. 521-540, pp. 540-547, pp. 559-566, 575-581 and pp. 581-587; Michal, G (1999) Biochemical Pathways: An Atlas of Biochemistry and Molecular Biology, John Wiley and Sons; Fallon, A. et al. (1987) Applications of HPLC in Biochemistry in: Laboratory Techniques in Biochemistry and Molecular Biology, vol. 17.

[0114.0.0.0] Fine chemicals like amino acids can for excample be detected advantageously via HPLC separation in ethanolic extract as described by Geigenberger et al. (Plant Cell & Environ, 19, 1996: 43–55). Amino acids can be extracted with hot water. After filtration the extracts are diluted with water containing 20 mg/mL sodium acide. The separation and detection of the amino acids is performed using an anion exchange column and an electrochemical detector. Technical details can be taken from Y. Ding et al., 2002, Direct determination of free amino acids and sugars in green tea by anion-exchange chromatography with integrated pulsed amperometric detection, J Chromatogr A, (2002) 982; 237-244, or e.g. from Karchi et al., 1993, Plant J. 3: 721-727; Matthews MJ, 1997 (Lysine, threonine and methionine biosynthesis. In BK Singh, ed, Plant Amino Acids: Biochemistry and Biotechnology. Dekker, New York, pp 205-225; H Hesse and R Hoefgen. (2003) Molecular aspects of methionine biosynthesis. TIPS 8(259-262.

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[0115.0.0.0] In a preferred embodiment, the present invention relates to a process for the production of the fine chemical comprising or generating in an organism or a part thereof the expression of at least one nucleic acid molecule comprising a nucleic acid molecule selected from the group consisting of:

a) nucleic acid molecule encoding, preferably at least the mature form, of the polypeptide as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208,

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210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or a fragment thereof, which confers an increase in the amount of the fine chemical in an organism or a part thereof;

- nucleic acid molecule comprising, preferably at least the mature form, of the b) nucleic acid molecule as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 10 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 15 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 20 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393;
  - c) nucleic acid molecule whose sequence can be deduced from a polypeptide sequence encoded by a nucleic acid molecule of (a) or (b) as result of the degeneracy of the genetic code and conferring an increase in the amount of the fine chemical in an organism or a part thereof;
  - d) nucleic acid molecule encoding a polypeptide which has at least 50% identity with the amino acid sequence of the polypeptide encoded by the nucleic acid molecule of (a) to (c) and conferring an increase in the amount of the fine chemical in an organism or a part thereof;
- and a nucleic acid molecule which hybidizes with a nucleic acid molecule of (a) to (c) under under stringent hybridisation conditions and conferring an increase in the amount of the fine chemical in an organism or a part thereof;
- f) nucleic acid molecule encoding a polypeptide, the polypeptide being derived by substituting, deleting and/or adding one or more amino acids of the amino acid sequence of the polypeptide encoded by the nucleic acid molecules (a) to (d), preferably to (a) to (c) and conferring an increase in the amount of the fine chemical in an organism or a part thereof;

- g) nucleic acid molecule encoding a fragment or an epitope of a polypeptide which
  is encoded by one of the nucleic acid molecules of (a) to (e), preferably to (a) to
  (c) and conferring an increase in the amount of the fine chemical in an organism
  or a part thereof;
- 5 h) nucleic acid molecule comprising a nucleic acid molecule which is obtained by amplifying nucleic acid molecules from a cDNA library or a genomic library using the primers as depicted in SEQ ID NO: 53 or SEQ ID NO: 54 and conferring an increase in the amount of the fine chemical in an organism or a part thereof;
- i) nucleic acid molecule encoding a polypeptide which is isolated, e.g. from an expression library, with the aid of monoclonal antibodies against a polypeptide encoded by one of the nucleic acid molecules of (a) to (h), preferably to (a) to (c), and and conferring an increase in the amount of the fine chemical in an organism or a part thereof;
- j) nucleic acid molecule which encodes a polypeptide comprising the consensus sequence as depicted in SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 397, SEQ ID NO: 398, SEQ ID NO: 399 and/or SEQ ID NO: 400 and conferring an increase in the amount of the fine chemical in an organism or a part thereof; and/or
- k) nucleic acid molecule which is obtainable by screening a suitable library under stringent conditions with a probe comprising one of the sequences of the nucleic acid molecule of (a) to (j), preferably to (a) to (c), or with a fragment of at least 15 nt, preferably 20 nt, 30 nt, 50 nt, 100 nt, 200 nt or 500 nt of the nucleic acid molecule characterized in (a) to (j), preferably to (a) to (c), and conferring an increase in the amount of the fine chemical in an organism or a part thereof;
- or which comprises a sequence which is complementary thereto.
- [0116.0.0.0] In one embodiment, the nucleic acid molecule used in the process distinguishes over the sequence as depicted in SEQ ID NO: 1, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 by one or more nucleotides or does not consist of the sequence as depicted in SEQ ID NO: 1, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75,

77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 5 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393. In one embodiment, the nucleic acid molecule of the present invention 10 is less than 100%, 99,999%, 99,99%, 99,9% or 99% identical to the sequence as depicted in SEQ ID NO: 1, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 15 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 20 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393. In another embodiment, the nucleic acid molecule does not encode a polypeptide of the sequence as depicted in SEQ ID NO: 2, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 25 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 30 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394. In another embodiment, the nucleic acid molecule does not encode a polypeptide of the sequence of the present invention is less than 100%, 99,999%, 99,99%, 99,9% or 99% identical to the sequence as depicted in SEQ ID NO: 2, 56, 58, 35 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 40 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306,

308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394. In another embodiment, the nucleic acid molecule encodes a polypeptide of the sequence as depicted in SEQ ID NO: 2, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 5 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 10 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 and distinguishes over said sequence by one or more amino acids preferably by 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids. In further another advantageously embodiment, the nucleic acid molecule used in the process distinguishes over the sequence as depicted in SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, 20 SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, SEQ ID NO: 41 SEQ ID NO: 43 or SEQ ID NO: 45 by one or more nucleotides or does not consist of the sequence as depicted in SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, 25 SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, SEQ ID NO: 41 SEQ ID NO: 43 or SEQ ID NO: 45. In one advantageously embodiment, the nucleic acid molecule of the present invention is less than 100%, 99,999%, 99,99%, 99,9% or 99% identical to the sequence as depicted in SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 30 17. SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, SEQ ID NO: 41 SEQ ID NO: 43 or SEQ ID NO: 45. In another advantageously embodiment, the nucleic acid molecule does not encode a polypeptide of the sequence as depicted in SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID 35 NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 40, SEQ ID NO: 42, SEQ ID NO: 44 or SEQ ID NO: 46.

40 [0117.0.0.0] Unless otherwise specified, the terms "polynucleotides", "nucleic acid" and "nucleic acid molecule" are interchangeably in the present context. Unless

otherwise specified, the terms "peptide", "polypeptide" and "protein" are interchangeably in the present context. The term "sequence" may relate to polynucleotides, nucleic acids, nucleic acid molecules, peptides, polypeptides and proteins, depending on the context in which the term "sequence" is used. The terms "gene(s)", "polynucleotide", "nucleic acid sequence", "nucleotide sequence", or "nucleic acid molecule(s)" as used herein refers to a polymeric form of nucleotides of any length, either ribonucleotides or deoxyribonucleotides. The terms refer only to the primary structure of the molecule.

[0118.0.0.0] Thus, the terms "gene(s)", "polynucleotide", "nucleic acid sequence",

"nucleotide sequence", or "nucleic acid molecule(s)" as used herein include doubleand single-stranded DNA and RNA. They also include known types of modifications, for
example, methylation, "caps", substitutions of one or more of the naturally occurring
nucleotides with an analog. Preferably, the DNA or RNA sequence of the invention
comprises a coding sequence encoding the herein defined polypeptide.

15 [0119.0.0.0] A "coding sequence" is a nucleotide sequence, which is transcribed into mRNA and/or translated into a polypeptide when placed under the control of appropriate regulatory sequences. The boundaries of the coding sequence are determined by a translation start codon at the 5'-terminus and a translation stop codon at the 3'-terminus. A coding sequence can include, but is not limited to mRNA, cDNA, recombinant nucleotide sequences or genomic DNA, while introns may be present as well under certain circumstances.

[0120.0.0.0] Nucleic acid molecules with the sequence as depicted in SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 17, SEQ ID NO: 19, SEQ ID NO: 21, SEQ ID NO: 23, SEQ ID NO: 25, SEQ ID NO: 27, SEQ ID NO: 29, SEQ ID NO: 31, SEQ ID 25 NO: 33, SEQ ID NO: 35, SEQ ID NO: 37, SEQ ID NO: 39, SEQ ID NO: 41 SEQ ID NO: 43 or SEQ ID NO: 45, nucleic acid molecules which are derived from the amino acid sequences as depicted in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 28, 30 SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID NO: 38, SEQ ID NO: 40, SEQ ID NO: 42, SEQ ID NO: 44 or SEQ ID NO: 46 or from polypeptides comprising the consensus sequence as depicted in SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID 35 NO: 397, SEQ ID NO: 398, SEQ ID NO: 399 and/or SEQ ID NO: 400, or their derivatives or homologues encoding polypeptides with the enzymatic or biological activity of a protein as depicted in SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 22, SEQ ID NO: 24, SEQ ID NO: 26, SEQ ID NO: 28, SEQ ID NO: 30, SEQ ID NO: 32, SEQ ID NO: 34, SEQ ID NO: 36, SEQ ID 40

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NO: 38, SEQ ID NO: 40, SEQ ID NO: 42, SEQ ID NO: 44 or SEQ ID NO: 46 and/or conferring a fine chemical increase after increasing its expression or activity are advantageously increased in the process according to the invention.

[0121.0.0.0] In one embodiment, said sequences are cloned into nucleic acid constructs, either individually or in combination. These nucleic acid constructs enable an optimal synthesis of the fine chemical produced in the process according to the invention.

[0122.0.0.0] Nucleic acid molecules, which are advantageous for the process according to the invention and which encode polypeptides with the biological activity of the protein of the invention can be determined from generally accessible databases.

[0123.0.0.0] Those, which must be mentioned, in particular in this context are general gene databases such as the EMBL database (Stoesser G. et al., Nucleic Acids Res 2001, Vol. 29, 17-21), the GenBank database (Benson D.A. et al., Nucleic Acids Res 2000, Vol. 28,15-18), or the PIR database (Barker W. C. et al., Nucleic Acids Res.

- 15 1999, Vol. 27, 39-43). It is furthermore possible to use organism-specific gene databases for determining advantageous sequences, in the case of yeast for example advantageously the SGD database (Cherry J. M. et al., Nucleic Acids Res. 1998, Vol. 26, 73-80) or the MIPS database (Mewes H.W. et al., Nucleic Acids Res. 1999, Vol. 27, 44-48), in the case of E. coli the GenProtEC database
- 20 (http://web.bham.ac.uk/bcm4ght6/res.html), and in the case of Arabidopsis the TAIR-database (Huala, E. et al., Nucleic Acids Res. 2001 Vol. 29(1), 102-5) or the MIPS database.

The nucleic acid molecules used in the process according to the [0124.0.0.0] invention take the form of isolated nucleic acid sequences, which encode polypeptides having the biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 25 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 30 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 35 378, 380, 382, 384, 386, 388, 390, 392 or 394and conferring the fine chemical increase.

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**[0125.0.0.0]** The nucleic acid sequence(s) used in the process for the production of the fine chemical in transgenic organisms originate advantageously from an eukaryote but may also originate from a prokaryote or an archebacterium, thus it can derived from e.g. a microorganism, an animal or a plant.

5 **[0126.0.0.0]** For the purposes of the invention, as a rule the plural is intended to encompass the singular and vice versa.

[0127.0.0.0] In order to improve the introduction of the nucleic acid sequences and the expression of the sequences in the transgenic organisms, which are used in the process, the nucleic acid sequences are incorporated into a nucleic acid construct and/or a vector. In addition to the herein described sequences which are used in the process according to the invention, further nucleic acid sequences, advantageously of biosynthesis genes of amino acids, carbohydrates, lipids, fatty acids, vitamins etc. produced in the process according to the invention, may additionally be present in the nucleic acid construct or in the vector and may be introduced into the organism together. However, these additional sequences may also be introduced into the organisms via other, separate nucleic acid constructs or vectors.

[0128.0.0.0] Using the herein mentioned cloning vectors and transformation methods such as those which are published and cited in: Plant Molecular Biology and Biotechnology (CRC Press, Boca Raton, Florida), chapter 6/7, pp. 71-119 (1993); F.F. White, Vectors for Gene Transfer in Higher Plants; in: Transgenic Plants, vol. 1, 20 Engineering and Utilization, Ed.: Kung and R. Wu, Academic Press, 1993, 15-38; B. Jenes et al., Techniques for Gene Transfer, in: Transgenic Plants, vol. 1, Engineering and Utilization, Ed.: Kung and R. Wu, Academic Press (1993), 128-143; Potrykus, Annu. Rev. Plant. Physiol. Plant Molec. Biol. 42 (1991), 205-225)) and further cited below, the nucleic acids may be used for the recombinant modification of a wide 25 range of organisms, in particular prokaryotic or eukaryotic microorganisms or plants, so that they become a better and more efficient producer of the fine chemical produced in the process according to the invention. This improved production, or production efficiency, of the fine chemical or products derived there from, such as modified proteins, can be brought about by a direct effect of the manipulation or by an indirect 30 effect of this manipulation.

[0129.0.0.0] In one embodiment, the nucleic acid molecule according to the invention originates from a plant, such as a plant selected from the families Aceraceae, Anacardiaceae, Apiaceae, Asteraceae, Brassicaceae, Cactaceae, Cucurbitaceae, Euphorbiaceae, Fabaceae, Malvaceae, Nymphaeaceae, Papaveraceae, Rosaceae, Salicaceae, Solanaceae, Arecaceae, Bromeliaceae, Cyperaceae, Iridaceae, Liliaceae, Orchidaceae, Gentianaceae, Labiaceae, Magnoliaceae, Ranunculaceae, Carifolaceae, Rubiaceae, Scrophulariaceae, Caryophyllaceae, Ericaceae, Polygonaceae, Violaceae, Juncaceae or Poaceae and preferably from a plant selected from the group of the

families Apiaceae, Asteraceae, Brassicaceae, Cucurbitaceae, Fabaceae, Papaveraceae, Rosaceae, Solanaceae, Liliaceae or Poaceae. Preferred are crop plants and in particular plants mentioned herein above as host plants such as the families and genera mentioned above for example preferred the species Anacardium occidentale. Calendula officinalis, Carthamus tinctorius, Cichorium intybus, Cynara 5 scolymus, Helianthus annus, Tagetes lucida, Tagetes erecta, Tagetes tenuifolia; Daucus carota; Corylus avellana, Corylus colurna, Borago officinalis; Brassica napus, Brassica rapa ssp., Sinapis arvensis Brassica juncea, Brassica juncea var. juncea, Brassica juncea var. crispifolia, Brassica juncea var. foliosa, Brassica nigra, Brassica sinapioides. Melanosinapis communis, Brassica oleracea, Arabidopsis thaliana, Anana 10 comosus, Ananas ananas, Bromelia comosa, Carica papaya, Cannabis sative, Ipomoea batatus, Ipomoea pandurata, Convolvulus batatas, Convolvulus tiliaceus, Ipomoea fastigiata, Ipomoea tiliacea, Ipomoea triloba, Convolvulus panduratus, Beta vulgaris, Beta vulgaris var. altissima, Beta vulgaris var. vulgaris, Beta maritima, Beta vulgaris var. perennis, Beta vulgaris var. conditiva, Beta vulgaris var. esculenta, 15 Cucurbita maxima, Cucurbita mixta, Cucurbita pepo, Cucurbita moschata, Olea europaea, Manihot utilissima, Janipha manihot,, Jatropha manihot., Manihot aipil, Manihot dulcis, Manihot manihot, Manihot melanobasis, Manihot esculenta, Ricinus communis, Pisum sativum, Pisum arvense, Pisum humile, Medicago sativa, Medicago falcata, Medicago varia, Glycine max Dolichos soja, Glycine gracilis, Glycine hispida, 20 Phaseolus max. Soja hispida, Soja max, Cocos nucifera, Pelargonium grossularioides, Oleum cocoas, Laurus nobilis, Persea americana, Arachis hypogaea, Linum usitatissimum, Linum humile, Linum austriacum, Linum bienne, Linum angustifolium, Linum catharticum, Linum flavum, Linum grandiflorum, Adenolinum grandiflorum, Linum lewisii, Linum narbonense, Linum perenne, Linum perenne var. lewisii, Linum 25 pratense, Linum trigynum, Punica granatum, Gossypium hirsutum, Gossypium arboreum, Gossypium barbadense, Gossypium herbaceum, Gossypium thurberi, Musa nana, Musa acuminata, Musa paradisiaca, Musa spp., Elaeis guineensis, Papaver orientale, Papaver rhoeas, Papaver dubium, Sesamum indicum, Piper aduncum, Piper amalago, Piper angustifolium, Piper auritum, Piper betel, Piper cubeba, Piper longum, 30 Piper nigrum, Piper retrofractum, Artanthe adunca, Artanthe elongata, Peperomia elongata, Piper elongatum, Steffensia elongata, , Hordeum vulgare, Hordeum jubatum, Hordeum murinum, Hordeum secalinum, Hordeum distichon Hordeum aegiceras, Hordeum hexastichon., Hordeum hexastichum, Hordeum irregulare, Hordeum sativum, Hordeum secalinum, Avena sativa, Avena fatua, Avena byzantina, Avena fatua var. 35 sativa, Avena hybrida, Sorghum bicolor, Sorghum halepense, Sorghum saccharatum, Sorghum vulgare, Andropogon drummondii, Holcus bicolor, Holcus sorghum, Sorghum aethiopicum, Sorghum arundinaceum, Sorghum caffrorum, Sorghum cernuum, Sorghum dochna, Sorghum drummondii, Sorghum durra, Sorghum guineense, Sorghum lanceolatum, Sorghum nervosum, Sorghum saccharatum, Sorghum 40 subglabrescens, Sorghum verticilliflorum, Sorghum vulgare, Holcus halepensis, Sorghum miliaceum millet, Panicum militaceum, Zea mays, Triticum aestivum, Triticum durum, Triticum turgidum, Triticum hybernum, Triticum macha, Triticum sativum or Triticum vulgare, Cofea spp., Coffea arabica, Coffea canephora, Coffea liberica, Capsicum annuum, Capsicum annuum var. glabriusculum, Capsicum frutescens, Capsicum annuum, Nicotiana tabacum, Solanum tuberosum, Solanum melongena, Lycopersicon esculentum, Lycopersicon lycopersicum., Lycopersicon pyriforme, Solanum integrifolium, Solanum iycopersicum. Theobroma cacao or Camellia sinensis.

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- [0130.0.0.0] In one embodiment, the nucleic acid molecule sequence originates advantageously from a microorganism as mentioned above under host organism such as a fungus for example the genera Aspergillus, Penicillium or Claviceps or from yeasts such as the genera Pichia, Torulopsis, Hansenula, Schizosaccharomyces, Candida, Rhodotorula or Saccharomyces, very especially advantageously from the yeast of the family Saccharomycetaceae, such as the advantageous genus Saccharomyces and the very advantageous genus and species Saccharomyces cerevisiae for the production of the fine chemical in microorganims.
- [0131.0.0.0] The skilled worker knows other suitable sources for the production of fine chemicals, which present also useful nucleic acid molecule sources. They include in general all prokaryotic or eukaryotic cells, preferably unicellular microorganisms, such as fungi like the genus Claviceps or Aspergillus or gram-positive bacteria such as the genera Bacillus, Corynebacterium, Micrococcus, Brevibacterium, Rhodococcus,
   Nocardia, Caseobacter or Arthrobacter or gram-negative bacteria such as the genera Escherichia, Flavobacterium or Salmonella, or yeasts such as the genera Rhodotorula, Hansenula or Candida.
- [0132.0.0.0] Production strains which are especially advantageously selected in the process according to the invention are microorganisms selected from the group of the families Actinomycetaceae, Bacillaceae, Brevibacteriaceae, Corynebacteriaceae, 25 Enterobacteriacae, Gordoniaceae, Micrococcaceae, Mycobacteriaceae, Nocardiaceae, Pseudomonaceae, Rhizobiaceae, Streptomycetaceae, Chaetomiaceae, Choanephoraceae, Cryptococcaceae, Cunninghamellaceae, Demetiaceae, Moniliaceae, Mortierellaceae, Mucoraceae, Pythiaceae, Saccharomycetaceae, Saprolegniaceae, Schizosaccharomycetaceae, Sodariaceae, Sporobolomycetaceae, 30 Tuberculariaceae, Adelotheciaceae, Dinophyceae, Ditrichaceae and Prasinophyceaeor of the genera and species consisting of Hansenula anomala, Candida utilis, Claviceps purpurea, Bacillus circulans, Bacillus subtilis, Bacillus sp., Brevibacterium albidum, Brevibacterium album, Brevibacterium cerinum, Brevibacterium flavum, Brevibacterium glutamigenes, Brevibacterium iodinum, Brevibacterium ketoglutamicum, 35 Brevibacterium lactofermentum, Brevibacterium linens, Brevibacterium roseum, Brevibacterium saccharolyticum, Brevibacterium sp., Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium ammoniagenes, Corynebacterium glutamicum (= Micrococcus glutamicum), Coryne-

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bacterium melassecola, Corynebacterium sp. or Escherichia coli, specifically Escherichia coli K12 and its described strains.

[0133.0.0.0] However, it is also possible to use artificial sequences, which differ in one or more bases (= nucleotides) from the nucleic acid sequences found in organisms, or in one or more amino acid molecules from polypeptide sequences found in organisms, in particular from the polypeptide sequences as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 15 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or the functional homologues thereof as described herein, preferably conferring above-mentioned biological activity, i.e. conferring the fine chemical increase after increasing its activity, e.g. having the 20 biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 25 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 30 382, 384, 386, 388, 390, 392 or 394.

[0134.0.0.0] In the process according to the invention nucleic acid sequences can be used, which, if appropriate, contain synthetic, non-natural or modified nucleotide bases, which can be incorporated into DNA or RNA. Said synthetic, non-natural or modified bases can for example increase the stability of the nucleic acid molecule outside or inside a cell. The nucleic acid molecules of the invention can contain the same modifications as aforementioned.

[0135.0.0.0] As used in the present context the term "nucleic acid molecule" may also encompass the untranslated sequence located at the 3' and at the 5' end of the coding gene region, for example at least 500, preferably 200, especially preferably 100,

nucleotides of the sequence upstream of the 5' end of the coding region and at least 100, preferably 50, especially preferably 20, nucleotides of the sequence downstream of the 3' end of the coding gene region. It is often advantageous only to choose the coding region for cloning and expression purposes.

5 [0136.0.0.0] Preferably, the nucleic acid molecule used in the process according to the invention or the nucleic acid molecule of the invention is an isolated nucleic acid molecule.

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[0137.0.0.0] An "isolated" polynucleotide or nucleic acid molecule is separated from other polynucleotides or nucleic acid molecules, which are present in the natural source of the nucleic acid molecule. An isolated nucleic acid molecule may be a chromosomal fragment of several kb, or preferably, a molecule only comprising the coding region of the gene. Accordingly, an isolated nucleic acid molecule of the invention may comprise chromosomal regions, which are adjacent 5' and 3' or further adjacent chromosomal regions, but preferably comprises no such sequences which naturally flank the nucleic acid molecule sequence in the genomic or chromosomal context in the organism from which the nucleic acid molecule originates (for example sequences which are adjacent to the regions encoding the 5'-3 and 3'-UTRs of the nucleic acid molecule). In various embodiments, the isolated nucleic acid molecule used in the process according to the invention may, for example comprise less than approximately 5 kb, 4 kb, 3 kb, 2 kb, 1 kb, 0.5 kb or 0.1 kb nucleotide sequences which naturally flank the nucleic acid molecule in the genomic DNA of the cell from which the nucleic acid molecule originates.

[0138.0.0.0] The nucleic acid molecules used in the process, for example the polynucleotides of the invention or of a part thereof can be isolated using molecular-biological standard techniques and the sequence information provided herein. Also, for example a homologous sequence or homologous, conserved sequence regions at the DNA or amino acid level can be identified with the aid of comparison algorithms. The former can be used as hybridization probes under standard hybridization techniques (for example those described in Sambrook et al., Molecular Cloning: A Laboratory Manual. 2nd Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989) for isolating further nucleic acid sequences useful in this process.

[0139.0.0.0] A nucleic acid molecule encompassing a complete sequence of the nucleic acid molecules used in the process, for example the polynucleotide of the invention, or a part thereof may additionally be isolated by polymerase chain reaction, oligonucleotide primers based on this sequence or on parts thereof being used. For example, a nucleic acid molecule comprising the complete sequence or part thereof can be isolated by polymerase chain reaction using oligonucleotide primers which have been generated on the basis of this sequence for example, mRNA can be isolated from

cells (for example by means of the guanidinium thiocyanate extraction method of Chirgwin et al. (1979) Biochemistry 18:5294-5299) and cDNA can be generated by means of reverse transcriptase (for example Moloney MLV reverse transcriptase, available from Gibco/BRL, Bethesda, MD, or AMV reverse transcriptase, obtainable from Seikagaku America, Inc., St.Petersburg, FL).

[0140.0.0.0] Synthetic oligonucleotide primers for the amplification, e.g. as shown in SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 395 or SEQ ID NO: 396, by means of polymerase chain reaction can be generated on the basis of a sequence shown herein, for example the sequence as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 10 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 15 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393. 20

[0141.0.0.0] Moreover, it is possible to identify conserved regions from various organisms by carrying out protein sequence alignments with the polypeptide used in the process of the invention, in particular with sequences of the polypeptide of the invention, from which conserved regions, and in turn, degenerate primers can be derived. Conserved regions are those, which show a very little variation in the amino acid in one particular position of several homologs from different origin. The consenus sequences as depicted in SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 397, SEQ ID NO: 398, SEQ ID NO: 399 and/or SEQ ID NO: 400 are derived from said alignments.

[0142.0.0.0] Degenerated primers can then be utilized by PCR for the amplification of fragments of novel proteins having above-mentioned activity, e.g. conferring the increase of the fine chemical after increasing the expression or activity or having the biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278,

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[0143.0.0.0] These fragments can then be utilized as hybridization probe for isolating the complete gene sequence. As an alternative, the missing 5' and 3' sequences can be isolated by means of RACE-PCR (rapid amplification of cDNA ends). A nucleic acid molecule according to the invention can be amplified using cDNA or, as an alternative, 10 genomic DNA as template and suitable oligonucleotide primers, following standard PCR amplification techniques. The nucleic acid molecule amplified thus can be cloned into a suitable vector and characterized by means of DNA sequence analysis. Oligonucleotides, which correspond to one of the nucleic acid molecules used in the process can be generated by standard synthesis methods, for example using an automatic DNA synthesizer.

[0144.0.0.0] Nucleic acid molecules which are advantageously for the process according to the invention can be isolated based on their homology to the nucleic acid molecules disclosed herein using the sequences or part thereof as hybridization probe and following standard hybridization techniques under stringent hybridization conditions. In this context, it is possible to use, for example, isolated nucleic acid 20 molecules of at least 15, 20, 25, 30, 35, 40, 50, 60 or more nucleotides, preferably of at least 15, 20 or 25 nucleotides in length which hybridize under stringent conditions with the above-described nucleic acid molecules, in particular with those which encompass a nucleotide sequence of the nucleic acid molecule used in the process of the invention or encoding a protein used in the invention or of the nucleic acid molecule of the 25 invention. Nucleic acid molecules with 30, 50, 100, 250 or more nucleotides may also be used.

[0145.0.0.0] The term "homology" means that the respective nucleic acid molecules or encoded proteins are functionally and/or structurally equivalent. The nucleic acid molecules that are homologous to the nucleic acid molecules described above and that are derivatives of said nucleic acid molecules are, for example, variations of said nucleic acid molecules which represent modifications having the same biological function, in particular encoding proteins with the same or substantially the same biological function. They may be naturally occurring variations, such as sequences from other plant varieties or species, or mutations. These mutations may occur naturally or may be obtained by mutagenesis techniques. The allelic variations may be naturally occurring allelic variants as well as synthetically produced or genetically engineered variants. Structurally equivalents can, for example, be identified by testing the binding of said polypeptide to antibodies or computer based predictions.

Structurally equivalent have the similar immunological characteristic, e.g. comprise similar epitopes.

**[0146.0.0.0]** By "hybridizing" it is meant that such nucleic acid molecules hybridize under conventional hybridization conditions, preferably under stringent conditions such as described by, e.g., Sambrook (Molecular Cloning; A Laboratory Manual, 2nd Edition, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY (1989)) or in Current Protocols in Molecular Biology, John Wiley & Sons, N. Y. (1989), 6.3.1-6.3.6.

**[0147.0.0.0]** According to the invention, DNA as well as RNA molecules of the nucleic acid of the invention can be used as probes. Further, as template for the identification of functional homologues Northern blot assays as well as Southern blot assays can be performed. The Northern blot assay advantageously provides further informations about the expressed gene product: e.g. expression pattern, occurance of processing steps, like splicing and capping, etc. The Southern blot assay provides additional information about the chromosomal localization and organization of the gene encoding the nucleic acid molecule of the invention.

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[0148.0.0.0] A preferred, nonlimiting example of stringent hydridization conditions are hybridizations in 6 x sodium chloride/sodium citrate (= SSC) at approximately 45°C, followed by one or more wash steps in 0.2 x SSC, 0.1% SDS at 50 to 65°C, for example at 50°C, 55°C or 60°C. The skilled worker knows that these hybridization conditions differ as a function of the type of the nucleic acid and, for example when organic solvents are present, with regard to the temperature and concentration of the buffer. The temperature under "standard hybridization conditions" differs for example as a function of the type of the nucleic acid between 42°C and 58°C, preferably between 45°C and 50°C in an aqueous buffer with a concentration of 0.1 x 0.5 x, 1 x, 2x, 3x, 4x or 5 x SSC (pH 7.2). If organic solvent(s) is/are present in the abovementioned buffer, for example 50% formamide, the temperature under standard conditions is approximately 40°C, 42°C or 45°C. The hybridization conditions for DNA:DNA hybrids are preferably for example 0.1 x SSC and 20°C, 25°C, 30°C, 35°C, 40°C or 45°C, preferably between 30°C and 45°C. The hybridization conditions for DNA:RNA hybrids are preferably for example 0.1 x SSC and 30°C, 35°C, 40°C, 45°C, 50°C or 55°C, preferably between 45°C and 55°C. The abovementioned hybridization temperatures are determined for example for a nucleic acid approximately 100 bp (= base pairs) in length and a G + C content of 50% in the absence of formamide. The skilled worker knows to determine the hybridization conditions required with the aid of textbooks, for example the ones mentioned above, or from the following textbooks: Sambrook et al., "Molecular Cloning", Cold Spring Harbor Laboratory, 1989; Hames and Higgins (Ed.) 1985, "Nucleic Acids Hybridization: A Practical Approach", IRL Press at Oxford University Press, Oxford; Brown (Ed.) 1991, "Essential Molecular Biology: A Practical Approach", IRL Press at Oxford University Press, Oxford.

[0149.0.0.0] A further example of one such stringent hybridization condition is hybridization at 4XSSC at 65°C, followed by a washing in 0.1XSSC at 65°C for one hour. Alternatively, an exemplary stringent hybridization condition is in 50 % formamide, 4XSSC at 42°C. Further, the conditions during the wash step can be selected from the range of conditions delimited by low-stringency conditions 5 (approximately 2X SSC at 50°C) and high-stringency conditions (approximately 0.2X SSC at 50°C, preferably at 65°C) (20X SSC: 0.3M sodium citrate, 3M NaCl, pH 7.0). In addition, the temperature during the wash step can be raised from low-stringency conditions at room temperature, approximately 22°C, to higher-stringency conditions at approximately 65°C. Both of the parameters salt concentration and temperature can be 10 varied simultaneously, or else one of the two parameters can be kept constant while only the other is varied. Denaturants, for example formamide or SDS, may also be employed during the hybridization. In the presence of 50% formamide, hybridization is preferably effected at 42°C. Relevant factors like i) length of treatment, ii) salt conditions, iii) detergent conditions, iv) competitor DNAs, v) temperature and vi) probe 15 selection can be combined case by case so that not all possibilities can be mentioned herein.

Thus, in a preferred embodiment, Northern blots are prehybridized with Rothi-Hybri-Quick buffer (Roth, Karlsruhe) at 68°C for 2h. Hybridzation with radioactive labelled probe is done overnight at 68°C. Subsequent washing steps are performed at 68°C with 1xSSC.

For Southern blot assays the membrane is prehybridized with Rothi-Hybri-Quick buffer (Roth, Karlsruhe) at 68°C for 2h. The hybridzation with radioactive labelled probe is conducted over night at 68°C. Subsequently the hybridization buffer is discarded and the filter shortly washed using 2xSSC; 0,1% SDS. After discarding the washing buffer new 2xSSC; 0,1% SDS buffer is added and incubated at 68°C for 15 minutes. This washing step is performed twice followed by an additional washing step using 1xSSC; 0,1% SDS at 68°C for 10 min.

[0150.0.0.0] Some further examples of conditions for DNA hybridization (Southern blot assays) and wash step are shown hereinbelow:

- (1) Hybridization conditions can be selected, for example, from the following conditions:
- a) 4X SSC at 65°C,

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- b) 6X SSC at 45°C,
- 35 c) 6X SSC, 100 mg/ml denatured fragmented fish sperm DNA at 68°C,
  - d) 6X SSC, 0.5% SDS, 100 mg/ml denatured salmon sperm DNA at 68°C,
  - e) 6X SSC, 0.5% SDS, 100 mg/ml denatured fragmented salmon sperm DNA, 50% formamide at 42°C,
  - f) 50% formamide, 4X SSC at 42°C,

- g) 50% (vol/vol) formamide, 0.1% bovine serum albumin, 0.1% Ficoll, 0.1% polyvinylpyrrolidone, 50 mM sodium phosphate buffer pH 6.5, 750 mM NaCl, 75 mM sodium citrate at 42°C,
- h) 2X or 4X SSC at 50°C (low-stringency condition), or
- 5 i) 30 to 40% formamide, 2X or 4X SSC at 42°C (low-stringency condition).
  - (2) Wash steps can be selected, for example, from the following conditions:
  - a) 0.015 M NaCl/0.0015 M sodium citrate/0.1% SDS at 50°C.
  - b) 0.1X SSC at 65°C.
- 10 c) 0.1X SSC, 0.5 % SDS at 68°C.
  - d) 0.1X SSC, 0.5% SDS, 50% formamide at 42°C.
  - e) 0.2X SSC, 0.1% SDS at 42°C.
  - f) 2X SSC at 65°C (low-stringency condition).

[0151.0.0.0] Polypeptides having above-mentioned biological activity, i.e. conferring the fine chemical increase, derived from other organisms, can be encoded by other 15 DNA sequences which hybridize to the sequences shown in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 20 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 25 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393under relaxed hybridization conditions and which code on expression for peptides having the fine chemical increasing activity.

[0152.0.0.0] Further, some applications have to be performed at low stringency hybridisation conditions, without any consequences for the specificity of the 30 hybridisation. For example, a Southern blot analysis of total DNA could be probed with a nucleic acid molecule of the present invention and washed at low stringency (55°C in 2xSSPE0, 1% SDS). The hybridisation analysis could reveal a simple pattern of only genes encoding polypeptides of the present invention or used in the process of the invention, e.g. having herein-mentioned activity of increasing the fine chemical. A 35 further example of such low-stringent hybridization conditions is 4XSSC at 50°C or hybridization with 30 to 40% formamide at 42°C. Such molecules comprise those which are fragments, analogues or derivatives of the polypeptide of the invention or used in the process of the invention and differ, for example, by way of amino acid and/or nucleotide deletion(s), insertion(s), substitution (s), addition(s) and/or recombination (s) 40 or any other modification(s) known in the art either alone or in combination from the

above-described amino acid sequences or their underlying nucleotide sequence(s). However, it is preferred to use high stringency hybridisation conditions.

[0153.0.0.0] Hybridization should advantageously be carried out with fragments of at least 5, 10, 15, 20, 25, 30, 35 or 40 bp, advantageously at least 50, 60, 70 or 80 bp, preferably at least 90, 100 or 110 bp. Most preferably are fragments of at least 15, 20, 25 or 30 bp. Preferably are also hybridizations with at least 100 bp or 200, very especially preferably at least 400 bp in length. In an especially preferred embodiment, the hybridization should be carried out with the entire nucleic acid sequence with conditions described above.

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10 [0154.0.0.0] The terms "fragment", "fragment of a sequence" or "part of a sequence" mean a truncated sequence of the original sequence referred to. The truncated sequence (nucleic acid or protein sequence) can vary widely in length; the minimum size being a sequence of sufficient size to provide a sequence with at least a comparable function and/or biological activity of the original sequence referred to or hybidizing with the nucleic acid molecule of the invention or used in the process of the invention under stringend conditions, while the maximum size is not critical. In some applications, the maximum size usually is not substantially greater than that required to provide the desired activity and/or function(s) of the original sequence.

[0155.0.0.0] Typically, the truncated amino acid sequence will range from about 5 to about 260 amino acids in length. More typically, however, the sequence will be a maximum of about 220 amino acids in length, preferably a maximum of about 215 or 100 amino acids. It is usually desirable to select sequences of at least about 100, 120 or 150 amino acids, up to a maximum of about 200 or 250 amino acids.

**[0156.0.0.0]** The term "epitope" relates to specific immunoreactive sites within an antigen, also known as antigenic determinates. These epitopes can be a linear array of monomers in a polymeric composition – such as amino acids in a protein – or consist of or comprise a more complex secondary or tertiary structure. Those of skill will recognize that immunogens (i.e., substances capable of eliciting an immune response) are antigens; however, some antigen, such as haptens, are not immunogens but may be made immunogenic by coupling to a carrier molecule. The term "antigen" includes references to a substance to which an antibody can be generated and/or to which the antibody is specifically immunoreactive.

[0157.0.0.0] In one embodiment the present invention relates to a epitope of the polypeptide of the present invention or used in the process of the present invention and conferring above mentioned biological activity, preferably conferring an increase in the fine chemical.

[0158.0.0.0] The term "one or several amino acids" relates to at least one amino acid but not more than that number of amino acids, which would result in a homology of

below 50% identity. Preferably, the identity is more than 70% or 80%, more preferred are 85%, 90%, 91%, 92%, 93%, 94% or 95%, even more preferred are 96%, 97%, 98%, or 99% identity.

[0159.0.0.0] Further, the nucleic acid molecule of the invention comprises a nucleic acid molecule, which is a complement of one of the nucleotide sequences of above 5 mentioned nucleic acid molecules or a portion thereof. A nucleic acid molecule which is complementary to one of the nucleotide sequences as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 10 \_ 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 15 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 367, 389, 391or 393 is one which is sufficiently complementary to one of the nucleotide sequences as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 25 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 30 385, 387, 389, 391or 393 such that it can hybridize to one of the nucleotide sequences as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 40 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393, thereby

forming a stable duplex. Preferably, the hybridisation is performed under stringent hybrization conditions. However, a complement of one of the herein disclosed sequences is preferably a sequence complement thereto according to the base pairing of nucleic acid molecules well known to the skilled person. For example, the bases A and G undergo base pairing with the bases T and U or C, resp. and visa versa. Modifications of the bases can influence the base-pairing partner.

[0160.0.0.0] The nucleic acid molecule of the invention comprises a nucleotide sequence which is at least about 30%, 35%, 40% or 45%, preferably at least about 50%, 55%, 60% or 65%, more preferably at least about 70%, 80%, or 90%, and even 10 more preferably at least about 95%, 97%, 98%, 99% most preferably at least about 99,1%; 99,2%, 99,3%; 99,4%; 99,5%; 99,6%; 99,7%; 99,8% or 99,9% or more homologous to a nucleotide sequence as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 15 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 20 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393, or a portion thereof and preferably has above mentioned biological activity, in particular having a fine chemical increasing activity after increasing the biological activity of a protein having the biological activity represented 25 by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 30 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 35 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 and their respective gene products.

[0161.0.0.0] The nucleic acid molecule of the invention comprises a nucleotide sequence which hybridizes, preferably hybridizes under stringent conditions as defined herein, to one of the nucleotide sequences as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65,

67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393, or a portion thereof and encodes a protein having above-mentioned biological activity, e.g. conferring the fine chemical increase, and optionally, having the biological activity of YNL090W.

Moreover, the nucleic acid molecule of the invention can comprise [0162.0.0.0] only a portion of the coding region of one of the sequences in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 15 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393, for example a fragment which can be used as a 25 probe or primer or a fragment encoding a biologically active portion of the polypeptide of the present invention or of a polypeptide used in the process of the present invention, i.e. having above-mentioned activity, e.g. conferring an increase of methionine if its activity is increased. The nucleotide sequences determined from the cloning of the present protein-according-to-the-invention-encoding gene allows for the 30 generation of probes and primers designed for use in identifying and/or cloning its homologues in other cell types and organisms. The probe/primer typically comprises substantially purified oligonucleotide. The oligonucleotide typically comprises a region of nucleotide sequence that hybridizes under stringent conditions to at least about 12, 15 preferably about 20 or 25, more preferably about 40, 50 or 75 consecutive nucleotides of a sense strand of one of the sequences set forth, e.g., in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 40 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203,

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[0163.0.0.0] Primer sets are interchangable. The person skilled in the art knows to combine said primers to result in the desired product, e.g. in a full-length clone or a partial sequence. Probes based on the sequences of the nucleic acid molecule of the invention or used in the process of the present invention can be used to detect transcripts or genomic sequences encoding the same or homologous proteins. The probe can further comprise a label group attached thereto, e.g. the label group can be a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor. Such

probes can be used as a part of a genomic marker test kit for identifying cells which express an polypepetide of the invention or used in the process of the present invention, such as by measuring a level of an encoding nucleic acid molecule in a sample of cells, e.g., detecting mRNA levels or determining, whether a genomic gene comprising the sequence of the polynucleotide of the invention or used in the processs of the present invention has been mutated or deleted.

[0164.0.0.0] The nucleic acid molecule of the invention encodes a polypeptide or portion thereof which includes an amino acid sequence which is sufficiently homologous to the amino acid sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 10 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 15 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 such that the protein or portion thereof maintains 20 the ability to participate in the fine chemical production, in particular an amino acid increasing activity as mentioned above or as described in the examples in plants or microorganisms is comprised.

[0165.0.0.0] As used herein, the language "sufficiently homologous" refers to proteins or portions thereof which have amino acid sequences which include a 25 minimum number of identical or equivalent amino acid residues (e.g., an amino acid residue which has a similar side chain as an amino acid residue in one of the sequences of the polypeptide of the present invention) to an amino acid sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 35 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 such that the protein or portion thereof is able to participate in the increase of the fine chemical 40 production. For examples having the biological activity represented by a protein as

depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 216, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 are described herein.

[0166.0.0.0] In one embodiment, the nucleic acid molecule of the present invention comprises a nucleic acid that encodes a portion of the present invention. The protein is at least about 30%, 35%, 40%, 45% or 50%, preferably at least about 15 55%, 60%, 65% or 70%, and more preferably at least about 75%, 80%, 85%, 90%, 91%, 92%, 93% or 94% and most preferably at least about 95%, 97%, 98%, 99% or more homologous to an entire amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 20 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 25 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 and having above-mentioned activity, e.g.conferring preferably the increase of the fine chemical. 30

[0167.0.0.0] Portions of proteins encoded by the nucleic acid molecule of the invention are preferably biologically active, preferably having above-mentioned annotated activity, e.g. conferring an increase of the fine chemical after increase of activity.

[0168.0.0.0] As mentioned herein, the term "biologically active portion" is intended to include a portion, e.g., a domain/motif, that confers increase of the fine chemical or has an immunological activity such that it is binds to an antibody binding specifially to the polypeptide of the present invention or a polypeptide used in the process of the present invention for producing the fine chemical;

The invention further relates to nucleic acid molecules that differ from [0169.0.0.0] one of the nucleotide sequences as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 5 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247. 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 10 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 (and portions thereof) due to degeneracy of the genetic code and thus encode a polypeptide of the present invention, in particular a polypeptide having above mentioned activity, e.g. conferring an increase in the fine chemical in a 15 organism. Advantageously, the nucleic acid molecule of the invention comprises, or in an other embodiment has, a nucleotide sequence encoding a protein comprising, or in an other embodiment having, an amino acid sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 20 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140. 142. 144. 146. 148. 150. 152. 154. 156. 158. 160. 162. 164. 166. 168. 170. 172. 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 25 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or the functional homologues. In a still further embodiment, the nucleic acid molecule of the invention encodes a full length 30 protein which is substantially homologous to an amino acid sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 35 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, - 40 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or the functional

homologues. However, in a preferred embodiment, the nucleic acid molecule of the present invention does not consist of the sequence as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393.

**[0170.0.0.0]** In addition, it will be appreciated by those skilled in the art that DNA sequence polymorphisms that lead to changes in the amino acid sequences may exist within a population. Such genetic polymorphism in the gene encoding the polypeptide of the invention or comprising the nucleic acid molecule of the invention may exist among individuals within a population due to natural variation.

- [0171.0.0.0] As used herein, the terms "gene" and "recombinant gene" refer to
  nucleic acid molecules comprising an open reading frame encoding the polypeptide of the invention or comprising the nucleic acid molecule of the invention or encoding the polypeptide used in the process of the present invention, preferably from a crop plant or from a microorgansim useful for the production of fine chemicals, in particular for the production of the fine chemical. Such natural variations can typically result in 1-5% variance in the nucleotide sequence of the gene. Any and all such nucleotide variations and resulting amino acid polymorphisms in genes encoding a polypeptide of the invention or comprising a the nucleic acid molecule of the invention that are the result of natural variation and that do not alter the functional activity as described are intended to be within the scope of the invention.
- [0172.0.0.0] Nucleic acid molecules corresponding to natural variants homologues of a nucleic acid molecule of the invention, which can also be a cDNA, can be isolated based on their homology to the nucleic acid molecules disclosed herein using the nucleic acid molecule of the invention, or a portion thereof, as a hybridization probe according to standard hybridization techniques under stringent hybridization conditions.
- [0173.0.0.0] Accordingly, in another embodiment, a nucleic acid molecule of the invention is at least 15, 20, 25 or 30 nucleotides in length. Preferably, it hybridizes under stringent conditions to a nucleic acid molecule comprising a nucleotide sequence of the nucleic acid molecule of the present invention or used in the process of the present invention, e.g. comprising the sequence as depicted in SEQ ID NO: 1, 3, 5, 7,

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9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393. The nucleic acid molecule is preferably at least 20, 30, 50, 100, 250 or more nucleotides in length.

[0174.0.0.0] The term "hybridizes under stringent conditions" is defined above. In one embodiment, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 30 %, 40 %, 50 % or 65% identical to each other typically remain hybridized to each other. Preferably, the conditions are such that sequences at least about 70%, more preferably at least about 75% or 80%, and even more preferably at least about 85%, 90% or 95% or more identical to each other typically remain hybridized to each other.

20 [0175.0.0.0] Preferably, nucleic acid molecule of the invention that hybridizes under stringent conditions to a sequence as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 25 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 30 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 corresponds to a naturally-occurring nucleic acid molecule of the invention. As used herein, a "naturally-occurring" nucleic acid molecule refers to an RNA or DNA molecule having a nucleotide sequence that occurs in nature (e.g., encodes a natural protein). Preferably, the nucleic acid molecule encodes a natural 35 protein having above-mentioned activity, e.g. conferring the fine chemical increase after increasing the expression or activity thereof or the activity of a protein of the invention or used in the process of the invention.

[0176.0.0.0] In addition to naturally-occurring variants of thesequences of the polypeptide or nucleic acid molecule of the invention as well as of the polypeptide or

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nucleic acid molecule used in the process of the invention that may exist in the population, the skilled artisan will further appreciate that changes can be introduced by mutation into a nucleotide sequence of the nucleic acid molecule encoding the polypeptide of the invention or used in the process of the present invention, thereby leading to changes in the amino acid sequence of the encoded polypeptide, without altering the functional ability of the polypeptide, preferably not decreasing said activity.

[0177.0.0.0] For example, nucleotide substitutions leading to amino acid substitutions at "non-essential" amino acid residues can be made in a sequence of the nucleic acid molecule of the invention or used in the process of the invention, e.g. in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 10 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 15 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393. 20

[0178.0.0.0] A"non-essential" amino acid residue is a residue that can be altered from the wild-type sequence of one without altering the activity of said polypeptide, whereas an "essential" amino acid residue is required for an activity as mentioned above, e.g. leading to an increase in the fine chemical in an organism after an increase of activity of the polypeptide. Other amino acid residues, however, (e.g., those that are not conserved or only semi-conserved in the domain having said activity) may not be essential for activity and thus are likely to be amenable to alteration without altering said activity.

[0179.0.0.0] Further, a person skilled in the art knows that the codon usage between organisms can differ. Therefore, he may adapt the codon usage in the nucleic acid molecule of the present invention to the usage of the organism in which the polynuclestide or polypeptide is expressed.

[0180.0.0.0] Accordingly, the invention relates to nucleic acid molecules encoding a polypeptide having above-mentioned biological activity, e.g. conferring an increase in the the fine chemical in an organism or part thereof that contain changes in amino acid residues that are not essential for said activity. Such polypeptides differ in amino acid sequence from a sequence contained in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114,

116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 5 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 yet retain said activity described herein. The nucleic acid molecule can comprise a nucleotide sequence encoding a polypeptide, wherein the 10 polypeptide comprises an amino acid sequence at least about 50% identical to an amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 15 · 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 20 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394and is capable of participation in the increase of production of the fine chemical after increasing its activity, e.g. its expression. Preferably, the protein encoded by the 25 nucleic acid molecule is at least about 60% identical to the sequence in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 30 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 35 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394, more preferably at least about 70% identical to one of the sequences in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 40 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216,

218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 5 388, 390, 392 or 394, even more preferably at least about 80%, 90%, 95% homologous to the sequence in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 10 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 15 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394, and most preferably at least about 96%, 97%, 98%, or 99% identical to the sequence in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 20 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 25 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394.

- [0181.0.0.0] To determine the percentage homology (= identity) of two amino acid sequences or of two nucleic acid molecules, the sequences are written one underneath the other for an optimal comparison (for example gaps may be inserted into the sequence of a protein or of a nucleic acid in order to generate an optimal alignment with the other protein or the other nucleic acid).
- [0182.0.0.0] The amino acid residues or nucleic acid molecules at the corresponding amino acid positions or nucleotide positions are then compared. If a position in one sequence is occupied by the same amino acid residue or the same nucleic acid molecule as the corresponding position in the other sequence, the molecules are homologous at this position (i.e. amino acid or nucleic acid "homology" as used in the present context corresponds to amino acid or nucleic acid "identity". The percentage homology between the two sequences is a function of the number of identical positions

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shared by the sequences (i.e. % homology = number of identical positions/total number of positions x 100). The terms "homology" and "identity" are thus to be considered as synonyms.

[0183.0.0.0] For the determination of the percentage homology (=identity) of two or more amino acids or of two or more nucleotide sequences several computer software programs have been developed. The homology of two or more sequences can be calculated with for example the software fasta, which presently has been used in the version fasta 3 (W. R. Pearson and D. J. Lipman (1988), Improved Tools for Biological Sequence Comparison.PNAS 85:2444-2448; W. R. Pearson (1990) Rapid and Sensitive Sequence Comparison with FASTP and FASTA, Methods in Enzymology 183:63 - 98; W. R. Pearson and D. J. Lipman (1988) Improved Tools for Biological Sequence Comparison.PNAS 85:2444- 2448; W. R. Pearson (1990); Rapid and Sensitive Sequence Comparison with FASTP and FASTAMethods in Enzymology 183:63 - 98). Another useful program for the calculation of homologies of different sequences is the standard blast program, which is included in the Biomax pedant software (Biomax, Munich, Federal Republic of Germany). This leads unfortunately sometimes to suboptimal results since blast does not always include complete sequences of the subject and the querry. Nevertheless as this program is very efficient it can be used for the comparison of a huge number of sequences. The following settings are typically used for such a comparisons of sequences: -p Program Name [String]; -d Database [String]; default = nr; -i Query File [File In]; default = stdin; -e Expectation value (E) [Real]; default = 10.0; -m alignment view options: 0 = pairwise; 1 = query-anchored showing identities; 2 = query-anchored no identities; 3 = flat query-anchored, show identities; 4 = flat query-anchored, no identities; 5 = query-anchored no identities and blunt ends; 6 = flat query-anchored, no identities and blunt ends; 7 = XML Blast output; 8 = tabular; 9 tabular with comment lines [Integer]; default = 0; -o BLAST report Output File [File Out] Optional; default = stdout; -F Filter query sequence (DUST with blastn, SEG with others) [String]; default = T; -G Cost to open a gap (zero invokes default behavior) [Integer]; default = 0; -E Cost to extend a gap (zero invokes default behavior) [Integer]; default = 0; -X X dropoff value for gapped alignment (in bits) (zero invokes default behavior); blastn 30, megablast 20, tblastx 0, all others 15 [Integer]; default = 0; -I Show GI's in deflines [T/F]; default = F; -q Penalty for a nucleotide mismatch (blastn only) [Integer]; default = -3; -r Reward for a nucleotide match (blastn only) [Integer]; default = 1; -v Number of database sequences to show one-line descriptions for (V) [Integer]; default = 500; -b Number of database sequence to show alignments for (B) [Integer]; default = 250; -f Threshold for extending hits, default if zero; blastp 11, blastn 0, blastx 12, tblastn 13; tblastx 13, megablast 0 [Integer]; default = 0; -g Perfom gapped alignment (not available with tblastx) [T/F]; default = T; -Q Query Genetic code to use [Integer]; default = 1; -D DB Genetic code (for tblast[nx] only) [Integer]; default = 1; -a Number

of processors to use [Integer]; default = 1; -O SeqAlign file [File Out] Optional; -J

Believe the query defline [T/F]; default = F; -M Matrix [String]; default = BLOSUM62; -W Word size, default if zero (blastn 11, megablast 28, all others 3) [Integer]; default = 0; -z Effective length of the database (use zero for the real size) [Real]; default = 0; -K Number of best hits from a region to keep (off by default, if used a value of 100 is recommended) [Integer]; default = 0; -P 0 for multiple hit, 1 for single hit [Integer]; 5 default = 0; -Y Effective length of the search space (use zero for the real size) [Real]; default = 0; -S Query strands to search against database (for blast[nx], and tblastx); 3 is both, 1 is top, 2 is bottom [Integer]; default = 3; -T Produce HTML output [T/F]; default = F; -I Restrict search of database to list of GI's [String] Optional; -U Use lower case filtering of FASTA sequence [T/F] Optional; default = F; -y X dropoff value 10 for ungapped extensions in bits (0.0 invokes default behavior); blastn 20, megablast 10, all others 7 [Real]; default = 0.0; -Z X dropoff value for final gapped alignment in bits (0.0 invokes default behavior); blastn/megablast 50, tblastx 0, all others 25 [Integer]; default = 0; -R PSI-TBLASTN checkpoint file [File In] Optional; -n MegaBlast search [T/F]; default = F; -L Location on query sequence [String] Optional; 15 -A Multiple Hits window size, default if zero (blastn/megablast 0, all others 40 [Integer]; default = 0; -w Frame shift penalty (OOF algorithm for blastx) [Integer]; default = 0; -t Length of the largest intron allowed in tblastn for linking HSPs (0 disables linking) [Integer]; default = 0.

[0184.0.0.0] Results of high quality are reached by using the algorithm of Needleman 20 and Wunsch or Smith and Waterman. Therefore programs based on said algorithms are preferred. Advantageously the comparisons of sequences can be done with the program PileUp (J. Mol. Evolution., 25, 351-360, 1987, Higgins et al., CABIOS, 5 1989: 151-153) or preferably with the programs Gap and BestFit, which are respectively based on the algorithms of Needleman and Wunsch [J. Mol. Biol. 48; 443-453 (1970)] 25 and Smith and Waterman [Adv. Appl. Math. 2; 482-489 (1981)]. Both programs are part of the GCG software-package [Genetics Computer Group, 575 Science Drive, Madison, Wisconsin, USA 53711 (1991); Altschul et al. (1997) Nucleic Acids Res. 25:3389 et seq.]. Therefore preferably the calculations to determine the perentages of sequence homology are done with the program Gap over the whole range of the 30 sequences. The following standard adjustments for the comparison of nucleic acid sequences were used: gap weight: 50, length weight: 3, average match: 10.000, average mismatch: 0.000.

[0185.0.0.0] For example a sequence which has a 80% homology with sequence SEQ ID NO: 1 at the nucleic acid level is understood as meaning a sequence which, upon comparison with the sequence SEQ ID NO: 1 by the above Gap program algorithm with the above parameter set, has a 80% homology.

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[0186.0.0.0] In the state of the art, homology between two polypeptides is also understood as meaning the identity of the amino acid sequence over in each case the entire sequence length which is calculated by comparison with the aid of the program

algorithm GAP (Wisconsin Package Version 10.0, University of Wisconsin, Genetics Computer Group (GCG), Madison, USA), setting the following parameters:

Gap weight: 8 Length weight: 2

Average match: 2,912 Average mismatch: -2,003

[0187.0.0.0] For example a sequence which has a 80% homology with sequence SEQ ID NO: 2 at the protein level is understood as meaning a sequence which, upon comparison with the sequence SEQ ID NO: 2 by the above program algorithm with the above parameter set, has a 80% homology.

[0188.0.0.0] Functional equivalents derived from one of the polypeptides as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 10 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 15 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 according to the 20 invention by substitution, insertion or deletion have at least 30%, 35%, 40%, 45% or 50%, preferably at least 55%, 60%, 65% or 70% by preference at least 80%, especially preferably at least 85% or 90%, 91%, 92%, 93% or 94%, very especially preferably at least 95%, 97%, 98% or 99% homology with one of the polypeptides as shown in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 25 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 30 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 according to the 35 invention and are distinguished by essentially the same properties as the polypeptide as shown in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 40

160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394.

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[0189.0.0.0] Functional equivalents derived from the nucleic acid sequence as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 10 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 15 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393according to the invention by substitution, insertion or deletion have at least 30%, 35%, 40%, 45% 20 or 50%, preferably at least 55%, 60%, 65% or 70% by preference at least 80%, especially preferably at least 85% or 90%, 91%, 92%, 93% or 94%, very especially preferably at least 95%, 97%, 98% or 99% homology with one of the polypeptides as shown in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 25 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 30 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 according to the invention and encode polypeptides having essentially the same properties as the 35 polypeptide as shown in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 40 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222,

224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394.

[0190.0.0.0] "Essentially the same properties" of a functional equivalent is above all understood as meaning that the functional equivalent has above mentioned acitivty, e.g conferring an increase in the fine chemical amount while increasing the amount of protein, activity or function of said functional equivalent in an organism, e.g. a microorgansim, a plant or plant or animal tissue, plant or animal cells or a part of the same.

[0191.0.0.0] A nucleic acid molecule encoding an homologous to a protein sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 15 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 20 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 can be created by introducing one or more nucleotide substitutions, additions or deletions into a 25 nucleotide sequence of the nucleic acid molecule of the present invention, in particular of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 30 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 35 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393such that one or more amino acid substitutions, additions or deletions are introduced into the encoded protein. Mutations can be introduced into the encoding sequences of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 40 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107,

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109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 by standard techniques, such as site-directed mutagenesis and PCR-mediated mutagenesis.

[0192.0.0.0] Preferably, conservative amino acid substitutions are made at one or more predicted non-essential amino acid residues. A "conservative amino acid substitution" is one in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine).

[0193.0.0.0] Thus, a predicted nonessential amino acid residue in a polypeptide of the invention or a polypeptide used in the process of the invention is preferably replaced with another amino acid residue from the same family. Alternatively, in another embodiment, mutations can be introduced randomly along all or part of a coding sequence of a nucleic acid molecule of the invention or used in the process of the invention, such as by saturation mutagenesis, and the resultant mutants can be screened for activity described herein to identify mutants that retain or even have increased above mentioned activity, e.g. conferring an increase in content of the fine chemical.

[0194.0.0.0] Following mutagenesis of one of the sequences of shown herein, the encoded protein can be expressed recombinantly and the activity of the protein can be determined using, for example, assays described herein (see Examples).

[0195.0.0.0] The highest homology of the nucleic acid molecule used in the process according to the invention was found for the following database entries by Gap search.

[0196.0.0.0] Homologues of the nucleic acid sequences used, with the sequence as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89,

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91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 5 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393, comprise also allelic variants with at least approximately 30%, 35%, 40% or 45% homology, by 10 preference at least approximately 50%, 60% or 70%, more preferably at least approximately 90%, 91%, 92%, 93%, 94% or 95% and even more preferably at least approximately 96%, 97%, 98%, 99% or more homology with one of the nucleotide sequences shown or the abovementioned derived nucleic acid sequences or their homologues, derivatives or analogues or parts of these. Allelic variants encompass in 15 particular functional variants which can be obtained by deletion, insertion or substitution of nucleotides from the sequences shown, preferably from SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 20 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 25 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393, or from the derived nucleic acid sequences, the intention being, however, that the enzyme activity or the biological activity of the resulting proteins synthesized is advantageously retained or increased. 30

[0197.0.0.0] In one embodiment of the present invention, the nucleic acid molecule of the invention or used in the process of the invention comprises the sequences shown in any of the sequences SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325,

327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393. It is preferred that the nucleic acid molecule comprises as little as possible other nucleotides not shown in any one of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 5 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 10 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393. In one embodiment, the nucleic acid molecule comprises less than 15 500, 400, 300, 200, 100, 90, 80, 70, 60, 50 or 40 further nucleotides. In a further embodiment, the nucleic acid molecule comprises less than 30, 20 or 10 further nucleotides. In one embodiment, the nucleic acid molecule use in the process of the invention is identical to the sequences shown in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 20 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 25 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393. 30

[0198.0.0.0] Also preferred is that the nucleic acid molecule used in the process of the invention encodes a polypeptide comprising the sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338,

340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394. In one embodiment, the nucleic acid molecule encodes less than 150, 130, 100, 80, 60, 50, 40 or 30 further amino acids. In a further embodiment, the encoded polypeptide comprises less than 20, 15, 10, 9, 8, 7, 6 or 5 further amino acids. In one embodiment used in the inventive process, the encoded polypeptide is identical to the sequences as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 10 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 15 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394.

[0199.0.0.0] In one embodiment, the nucleic acid molecule of the invention or used in the process encodes a polypeptide comprising the sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 20 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 25 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 and comprises less than 100 30 further nucleotides. In a further embodiment, said nucleic acid molecule comprises less than 30 further nucleotides. In one embodiment, the nucleic acid molecule used in the process is identical to a coding sequence of the sequences as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 35 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 40

273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305,

307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393.

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[0200.0.0.0] Polypeptides (= proteins), which still have the essential enzymatic activity of the polypeptide of the present invention conferring an increase of the fine chemical i.e. whose activity is essentially not reduced, are polypeptides with at least 10% or 20%, by preference 30% or 40%, especially preferably 50% or 60%, very especially preferably 80% or 90 or more of the wild type biological activity or enzyme activity, advantageously, the activity is essentially not reduced in comparison with the activity of a polypeptide as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 15 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 20 388, 390, 392 or 394 expressed under identical conditions.

[0201.0.0.0] Homologues of as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 25 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 30 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 also mean truncated sequences, cDNA, single-stranded DNA or RNA of the coding and noncoding DNA sequence. Homologues of said sequences are also understood as meaning derivatives, which comprise noncoding regions such as, 35 for example, UTRs, terminators, enhancers or promoter variants. The promoters upstream of the nucleotide sequences stated can be modified by one or more nucleotide substitution(s), insertion(s) and/or deletion(s) without, however, interfering with the functionality or activity either of the promoters, the open reading frame (= ORF) or with the 3'-regulatory region such as terminators or other 3'regulatory 40 regions, which are far away from the ORF. It is furthermore possible that the activity of

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the promoters is increased by modification of their sequence, or that they are replaced completely by more active promoters, even promoters from heterologous organisms. Appropriate promoters are known to the person skilled in the art and are mentioned herein below.

- 5 [0202.0.0.0] In a further embodiment, the process according to the present invention comprises the following steps:
  - (a) selecting an organism or a part thereof expressing the polypeptide of this invention;
  - (b) mutagenizing the selected organism or the part thereof;
- 10 (c) comparing the activity or the expression level of said polypeptide in the mutagenized organism or the part thereof with the activity or the expression of said polypeptide in the selected organisms or the part thereof;
  - (d) selecting the mutagenized organisms or parts thereof, which comprise an increased activity or expression level of said polypeptide compared to the selected organism (a) or the part thereof;
  - (e) optionally, growing and cultivating the organisms or the parts thereof; and
  - (f) recovering, and optionally isolating, the free or bound the fine chemical produced by the selected mutated organisms or parts thereof.
- [0203.0.0.0] The organisms or part thereof produce according to the herein mentioned process of the invention an increased level of free and/or protein-bound fine chemical compared to said control or selected organisms or parts thereof.
  - [0204.0.0.0] Advantageously the seclected organisms are mutagenized according to the invention. According to the invention mutagenesis is any change of the genetic information in the genom of an organism, that means any structural or compositional change in the nucleic acid preferably DNA of an organism that is not caused by normal segregation or genetic recombiantion processes. Such mutations may occur spontaneously, or may be induced by mutagens as described below. Such change can be induced either randomly or selectivly. In both cases the genetic information of the organism is modified. In general this lead to the situation that the activity of the gene product of the relevant genes inside the cells or inside the organism is increased.
  - [0205.0.0.0] In case of the specific or so called site directed mutagenesis a distinct gene is mutated and thereby its activity and/or the activity or the encoded gene product is repressed, reduced or increased, preferably increased. In the event of a random

mutagenesis one or more genes are mutated by chance and their activities and/or the activities of their gene productes are repressed, reduced or increased, preferably increased.

[0206.0.0.0] For the purpose of a mutagenesis of a huge population of organisms, such population can be transformed with a DNA construct, which is useful for the activation of as much as possible genes of an organism, preferably all genes. For example the construct can contain a strong promoter or one or more enhancers, which are capable of transcriptionally activate genes in the vicinity of their integration side. With this method it is possible to statistically mutagenize, eg activate nearly all genes of an organism by the random integration of an activation construct. Afterwards the skilled 10 . worker can identify those mutagenized lines in which a gene of the invention has been activated, which in turns leads to the desired increase in the fine chemical production.

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[0207.0.0.0] The genes of the invention can also be activated by mutagensis, either of regulatory or coding regions. In the event of a random mutagenesis a huge number of organisms are treated with a mutagenic agent. The amount of said agent and the intensity of the treatment will be chosen in such a manner that statistically nearly every gene is mutated once. The process for the random mutagensis as well as the respective agens is well known by the skilled person. Such methods are disclosed for example by A.M. van Harten [(1998), "Mutation breeding: theory and practical applications", Cambridge University Press, Cambridge, UKJ, E Friedberg, G Walker, W Siede [(1995), "DNA Repair and Mutagenesis", Blackwell Publishing], or K. Sankaranarayanan, J. M. Gentile, L. R. Ferguson [(2000) "Protocols in Mutagenesis", Elsevier Health Sciences]. As the skilled worker knows the spontaneous mutation rate in the cells of an organism is very low and that a large numer of chemical, physical or biological agents are available for the mutagenesis of organisms. These agents are named as mutagens or mutagenic agents. As mentioned before three different kinds of mutagens (chemical, physical or biological agents) are available.

[0208.0.0.0] There are different classes of chemical mutagens, which can be separated by their mode of action. For example base analogues such as 5bromouracil, 2-amino purin. Other chemical mutagens are interacting with the DNA such as sulphuric acid, nitrous acid, hydroxylamine; or other alkylating agents such as monofunctional agents like ethyl methanesulfonate, dimethylsulfate, methyl methanesulfonate), bifunctional like dichloroethyl sulphide, Mitomycin, Nitrosoguanidine – dialkylnitrosamine, N-Nitrosoguanidin derivatives, N-alkyl-N-nitro-Nnitroso-guanidine-), ntercalating dyes like Acridine, ethidium bromide).

[0209.0.0.0] Physical mutagens are for example ionizing irradiation (X ray), UV irradiation. Different forms of irradiation are available and they are strong mutagens. Two main classes of irradiation can be distinguished: a) non-ionizing irradiation such as UV light or ionizing irradiation such as X ray. Biological mutagens are for example

transposable elements for example IS elements such as IS100, transposons such as Tn5, Tn10, Tn916 or Tn1000 or phages like Mu<sup>amplac</sup>, P1, T5, λplac etc. Methods for introducing this phage DNA into the appropriate microorganism are well known to the skilled worker (see Microbiology, Third Edition, Eds. Davis, B.D., Dulbecco, R., Eisen, H.N. and Ginsberg, H.S., Harper International Edition, 1980). The common procedure of a transposon mutagenesis is the insertion of a transposable element within a gene or nearby for example in the promotor or terminator region and thereby leading to a loss of the gene function. Procedures to localize the transposon within the genome of the organisms are well known by a person skilled in the art.

10 [0210.0.0.0] Preferably a chemical or biochemical procedure is used for the mutagenesis of the organisms. A preferred chemical method is the mutagensis with Nmethyl-N-nitro-nitrosoguanidine.

[0211.0.0.0] Other biological methods are disclosed by Spee et al. (Nucleic Acids Research, Vol. 21, No. 3, 1993: 777 - 778). Spee et al. teaches a PCR method using dITP for the random mutagenesis. This method described by Spee et al. was further improved by Rellos et al. (Protein Expr. Purif., 5, 1994 : 270 - 277). The use of an in vitro recombination technique for molecular mutagenesis is described by Stemmer (Proc. Natl. Acad. Sci. USA, Vol. 91, 1994: 10747 - 10751). Moore et al. (Nature Biotechnology Vol. 14, 1996: 458 - 467) describe the combination of the PCR and recombination methods for increasing the enzymatic activity of an esterase toward a para-nitrobenzyl ester. Another route to the mutagenesis of enzymes is described by Greener et al. in Methods in Molecular Biology (Vol. 57, 1996: 375 - 385). Greener et al. use the specific Escherichia coli strain XL1-Red to generate Escherichia coli mutants, which have increased antibiotic resistance.

[0212.0.0.0] In one embodiment, the protein according to the invention or the nucleic acid molecule characterized herein originates from a eukaryotic or prokaryotic organism such as a non-human animal, a plant, a microorganism such as a fungus, yeast, an alga, a diatom or a bacterium. Nucleic acid molecules, which advantageously can be used in the process of the invention originate from yeasts, for example the family Saccharomycetaceae, in particular the genus Saccharomyces, or yeast genera such as Candida, Hansenula, Pichia, Yarrowia, Rhodotorula or Schizosaccharomyces and the especially advantageous from the species Saccharomyces cerevisiae.

[0213.0.0.0] In one embodiment, nucleic acid molecules, which advantageously can be used in the process of the invention originate from yeast, for example from Saccharomycetaceae, particularly from the genus Saccharomyces advantageously form the species Saccharomyces cerevisiae.

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[0214.0.0.0] If, in the process according to the invention, plants are selected as the donor organism, this plant may, in principle, be in any phylogenetic relation of the

- recipient plant. Donor and recipient plant may belong to the same family, genus, species, variety or line, resulting in an increasing homology between the nucleic acids to be integrated and corresponding parts of the genome of the recipient plant. This also applies analogously to microorganisms as donor and recipient organism.
- It might also be advantageously to use nuclei acids molecules from very distinct species, since these might exhibit reduced sensitivity against endogenous regulatory mechanisms and such sequences might not be recognized by endogenous silencing mechanisms.
- [0215.0.0.0] Accordingly, one embodiment of the application relates to the use of nucleic acid molecules in the process of the invention from plants, e.g. crop plants, e.g. from: B. napus; O. sativa, Glycine max; B. vulgaris, L. japonicus, Z. elegans, Z. mays, C. arietinum, A. thaliana, H. vulgare, N. tabacum, G. hirsutum, P. patens, F. distichus, sunflower linseed or maize or their homologues.
- [0216.0.0.0] Accordingly, in one embodiment, the invention relates to a nucleic acid molecule, which comprises a nucleic acid molecule selected from the group consisting of:
- nucleic acid molecule encoding of the polypeptide as depicted in SEQ ID NO: 2, a) 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 20 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 25 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394or a fragment thereof, which confers an increase in the amount of fine chemical in an organism or a part thereof; 30
  - b) nucleic acid molecule comprising of the nucleic acid molecule as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285,

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287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 or a fragment thereof, which confers an increase in the amount of fine chemical in an organism or a part thereof;

- c) nucleic acid molecule whose sequence can be deduced from a polypeptide sequence encoded by a nucleic acid molecule of (a) or (b) as a result of the degeneracy of the genetic code and conferring an increase in the amount of fine chemical in an organism or a part thereof;
- nucleic acid molecule which encodes a polypeptide which has at least 50% identity with the amino acid sequence of the polypeptide encoded by the nucleic acid molecule of (a) to (c) and conferring an increase in the amount of fine chemical in an organism or a part thereof;
- e) nucleic acid molecule which hybridizes with a nucleic acid molecule of (a) to (c)
  under stringent hybridization conditions and conferring an increase in the amount
  of fine chemical in an organism or a part thereof;
  - f) nucleic acid molecule encoding a polypeptide, the polypeptide being derived by substituting, deleting and/or adding one or more amino acids of the amino acid sequence of the polypeptide encoded by the nucleic acid molecules (a) to (d), preferably to (a) to (c), and conferring an increase in the amount of the fine chemical in an organism or a part thereof;
  - nucleic acid molecule encoding a fragment or an epitope of a polypeptide which
    is encoded by one of the nucleic acid molecules of (a) to (e), preferably to (a) to
    (c) and conferring an increase in the amount of the fine chemical in an organism
    or a part thereof;
  - h) nucleic acid molecule which encompasses a nucleic acid molecule which is obtained by amplifying nucleic acid molecules from a cDNA library or a genomic library using the primers in SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 395 or SEQ ID NO: 396 and conferring an increase in the amount of the fine chemical in an organism or a part thereof;
  - i) nucleic acid molecule encoding a polypeptide which is isolated, e.g. from a expression library, with the aid of monoclonal and/or polyclonal antibodies against a polypeptide encoded by one of the nucleic acid molecules of (a) to (g), preferably to (a) to (c) and conferring an increase in the amount of the fine chemical in an organism or a part thereof;

- nucleic acid molecule encoding a polypeptide comprising the consensus sequence as depicted in SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 397, SEQ ID NO: 398, SEQ ID NO: 399 and/or SEQ ID NO: 400 and conferring an increase in the amount of the fine chemical in an organism or a part thereof; and/or
- 5 nucleic acid molecule which is obtainable by screening a suitable nucleic acid k) library under stringent hybridization conditions with a probe comprising one of the sequences of the nucleic acid molecule of (a) to (k) or with a fragment of at least 15 nt, preferably 20 nt, 30 nt, 50 nt, 100 nt, 200 nt or 500 nt of the nucleic acid molecule characterized in (a) to (h) or of the nucleic acid molecule as depicted in 10 SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 15 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 20 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 or a nucleic acid molecule encoding, preferably at least the mature form of, the polypeptide as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 25 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 30 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394, and conferring an increase in the amount of the fine 35 chemical in an organism or a part thereof;

or which encompasses a sequence which is complementary thereto;

whereby, preferably, the nucleic acid molecule according to (a) to (k) distinguishes over the sequence as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79,

81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 5 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 by one or more nucleotides. In one embodiment, the nucleic acid molecule of the 10 invention does not consist of the sequence as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 15 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 20 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393. In an other embodiment, the nucleic acid molecule of the present invention is at least 30 % identical and less than 100%, 99,999%, 99,99%, 99,9% or 99% identical to the sequence as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 25 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 30 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393. In a further embodiment the nucleic acid 35 molecule does not encode the polypeptide sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 40 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240,

242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394. Accordingly, in one embodiment, the 5 nucleic acid molecule of the present invention encodes in one embodiment a polypeptide which differs at least in one or more amino acids from the polypeptide as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 10 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394. In another embodiment, the nucleic acid molecule as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 20 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 25 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 does not encode a protein of the sequence as 30 depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 35 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 40 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394. Accordingly, in one embodiment, the protein encoded by a sequences of a nucleic acid

accoriding to (a) to (k) does not consist of the sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 5 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 10 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394. In a further embodiment, the protein of the present invention is at least 30 % identical to protein sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 15 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 20 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 and less than 100%, preferably less than 99,999%, 99,99% or 99,9%, more preferably less than 25 99%, 98%, 97%, 96% or 95% identical to the sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 30 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 35 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394.

[0217.0.0.0] The nucleic acid sequences used in the process are advantageously introduced in a nucleic acid construct, preferably an expression cassette, which makes the expression of the nucleic acid molecules in an organism, advantageously a plant or a microorganism possible.

**[0218.0.0.0]** Accordingly, the invention also relates to a nucleic acid construct, preferably to an expression construct, comprising the nucleic acid molecule of the present invention functionally linked to one or more regulatory elements or signals.

[0219.0.0.0] As described herein, the nucleic acid construct can also comprise further genes, which are introduced into the organisms or cells. It is possible and 5 advantageous to introduce into, and express in, the host organisms regulatory genes such as genes for inductors, repressors or enzymes, which, owing to their enzymatic activity, engage in the regulation of one or more genes of a biosynthetic pathway. These genes can be of heterologous or homologous origin. Moreover, further biosynthesis genes may advantageously be present, or else these genes may be 10 located on one or more further nucleic acid constructs. Genes, which are advantageously employed as biosynthesis genes are genes of the amino acid metabolism, of glycolysis, of the tricarboxylic acid metabolism or their combinations. As described herein, regulator sequences or factors can have a positive effect on preferably the gene expression of the genes introduced, thus increasing it. Thus, an 15 enhancement of the regulator elements may advantageously take place at the transcriptional level by using strong transcription signals such as promoters and/or enhancers. In addition, however, an enhancement of translation is also possible, for example by increasing mRNA stability or by inserting a translation enhancer sequence.

[0220.0.0.0] In principle, the nucleic acid construct can comprise the herein described regulator sequences and further sequences relevant for the expression of the comprised genes. Thus, the nucleic acid construct of the invention can be used as expression cassette and thus can be used directly for introduction into the plant, or else they may be introduced into a vector. Accordingly in one embodiment the nucleic acid construct is an expression cassette comprising a microorganism promoter or a microorganism terminator or both. In another embodiment the expression cassette encompasses a plant promoter or a plant terminator or both.

[0221.0.0.0] Accordingly, in one embodiment, the process according to the invention comprises the following steps:

- 30 (a) introducing of a nucleic acid construct comprising the nucleic acid molecule of the invention or used in the process of the invention or encoding the polypeptide of the present invention or used in the process of the invention; or
- (b) introducing of a nucleic acid molecule, including regulatory sequences or factors, which expression increases the expression of the nucleic acid molecule of the invention or used in the process of the invention or encoding the polypeptide of the present invention or used in the process of the invention in a cell, or an organism or a part thereof, preferably in a plant, plant cell or a microorganism, and

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(c) expressing of the gene product encoded by the nucleic acid construct or the nucleic acid molecule mentioned under (a) or (b) in the cell or the organism.

[0222.0.0.0] After the introduction and expression of the nucleic acid construct the transgenic organism or cell is advantageously cultured and subsequently harvested. The transgenic organism or cell may be a prokaryotic or eukaryotic organism such as a microorganism, a non-human animal and plant for example a plant or animal cell, a plant or animal tissue, preferably a crop plant, or a part thereof.

[0223.0.0.0] To introduce a nucleic acid molecule into a nucleic acid construct, e.g. as part of an expression cassette, the codogenic gene segment is advantageously subjected to an amplification and ligation reaction in the manner known by a skilled person. It is preferred to follow a procedure similar to the protocol for the Pfu DNA polymerase or a Pfu/Taq DNA polymerase mixture. The primers are selected according to the sequence to be amplified. The primers should expediently be chosen in such a way that the amplificate comprise the codogenic sequence from the start to the stop codon. After the amplification, the amplificate is expediently analyzed. For example, the analysis may consider quality and quantity and be carried out following separation by gel electrophoresis. Thereafter, the amplificate can be purified following a standard protocol (for example Qiagen). An aliquot of the purified amplificate is then available for the subsequent cloning step. The skilled worker generally knows suitable cloning vectors.

[0224.0.0.0] They include, in particular, vectors which are capable of replication in easy to handle cloning systems like as bacterial yeast or insect cell based (e.g. baculovirus expression) systems, that is to say especially vectors which ensure efficient cloning in E. coli, and which make possible the stable transformation of plants. Vectors, which must be mentioned, in particular are various binary and cointegrated vector systems, which are suitable for the T-DNA-mediated transformation. Such vector systems are generally characterized in that they contain at least the vir genes, which are required for the Agrobacterium-mediated transformation, and the T-DNA border sequences.

[0225.0.0.0] In general, vector systems preferably also comprise further cisregulatory regions such as promoters and terminators and/or selection markers by means of which suitably transformed organisms can be identified. While vir genes and T-DNA sequences are located on the same vector in the case of cointegrated vector systems, binary systems are based on at least two vectors, one of which bears vir genes, but no T-DNA, while a second one bears T-DNA, but no vir gene. Owing to this fact, the last-mentioned vectors are relatively small, easy to manipulate and capable of replication in E. coli and in Agrobacterium. These binary vectors include vectors from the series pBIB-HYG, pPZP, pBecks, pGreen. Those, which are preferably used in accordance with the invention, are Bin19, pBI101, pBinAR, pGPTV and pCAMBIA. An

overview of binary vectors and their use is given by Hellens et al, Trends in Plant Science (2000) 5, 446–451.

[0226.0.0.0] For a vector preparation, vectors may first be linearized using restriction endonuclease(s) and then be modified enzymatically in a suitable manner. Thereafter, the vector is purified, and an aliquot is employed in the cloning step. In the cloning step, the enzyme-cleaved and, if required, purified amplificate is cloned together with similarly prepared vector fragments, using ligase. In this context, a specific nucleic acid construct, or vector or plasmid construct, may have one or else more codogenic gene segments. The codogenic gene segments in these constructs are preferably linked operably to regulatory sequences. The regulatory sequences include, in particular, plant sequences like the above-described promoters and terminators. The constructs can advantageously be propagated stably in microorganisms, in particular Escherichia coli and/or Agrobacterium tumefaciens, under selective conditions and enable the transfer of heterologous DNA into plants or other microorganisms. In accordance with a particular embodiment, the constructs are based on binary vectors (overview of a 15 binary vector: Hellens et al., 2000). As a rule, they contain prokaryotic regulatory sequences, such as replication origin and selection markers, for the multiplication in microorganisms such as Escherichia coli and Agrobacterium tumefaciens. Vectors can further contain agrobacterial T-DNA sequences for the transfer of DNA into plant genomes or other eukaryotic regulatory sequences for transfer into other eukaryotic 20 cells, e.g. Saccharomyces sp. or other prokaryotic regulatory sequences for the transfer into other prokaryotic cells, e.g. Corynebacterium sp. or Bacillus sp. For the transformation of plants, the right border sequence, which comprises approximately 25 base pairs, of the total agrobacterial T-DNA sequence is advantageously included. Usually, the plant transformation vector constructs according to the invention contain 25 T-DNA sequences both from the right and from the left border region, which contain expedient recognition sites for site-specific acting enzymes, which, in turn, are encoded by some of the vir genes.

[0227.0.0.0] Suitable host organisms are known to the skilled worker. Advantageous organisms are described further above in the present application. They include in 30 particular eukaryotes or eubacteria, e.g. prokaryotes or archae bacteria. Advantageously host organisms are microorganisms selected from the group consisting of Actinomycetaceae, Bacillaceae, Brevibacteriaceae, Corynebacteriaceae, Enterobacteriacae, Gordoniaceae, Micrococcaceae, Mycobacteriaceae, Nocardiaceae, Pseudomonaceae, Rhizobiaceae, Streptomycetaceae, Chaetomiaceae, 35 Choanephoraceae, Cryptococcaceae, Cunninghamellaceae, Demetiaceae, Moniliaceae, Mortierellaceae, Mucoraceae, Pythiaceae, Saccharomycetaceae, Saprolegniaceae, Schizosaccharomycetaceae, Sodariaceae, Sporobolomycetaceae, Tuberculariaceae, Adelotheciaceae, Dinophyceae, Ditrichaceae and Prasinophyceae. Preferably are unicellular, microorganisms, e.g. fungi, bacteria or protoza, such as 40 fungi like the genus Claviceps or Aspergillus or gram-positive bacteria such as the

genera Bacillus, Corynebacterium, Micrococcus, Brevibacterium, Rhodococcus, Nocardia, Caseobacter or Arthrobacter or gram-negative bacteria such as the genera Escherichia, Flavobacterium or Salmonella, or yeasts such as the genera Rhodotorula, Hansenula, Pichia, Yerrowia, Saccharomyces, Schizosaccharomyces or Candida.

- [0228.0.0.0] Host organisms which are especially advantageously selected in the process according to the invention are microorganisms selected from the group of the genera and species consisting of Hansenula anomala, Saccharomyces cerevisiae, Candida utilis, Claviceps purpurea, Bacillus circulans, Bacillus subtilis, Bacillus sp., Brevibacterium albidum, Brevibacterium album, Brevibacterium cerinum,
- Brevibacterium flavum, Brevibacterium glutamigenes, Brevibacterium iodinum, Brevibacterium ketoglutamicum, Brevibacterium lactofermentum, Brevibacterium linens, Brevibacterium roseum, Brevibacterium saccharolyticum, Brevibacterium sp., Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium ammoniagenes, Corynebacterium glutamicum (= Micrococcus glutamicum), Corynebacterium melassecola, Corynebacterium sp. or Escherichia coli, specifically Saccharomyces cerevisiae or Escherichia coli K12 and its described strains.
- [0229.0.0.0] Advantageously preferred in accordance with the invention are host organisms of the genus Agrobacterium tumefaciens or plants. Preferred plants are selected from among the families Aceraceae, Anacardiaceae, Apiaceae, Asteraceae, Apiaceae, Betulaceae, Boraginaceae, Brassicaceae, Bromeliaceae, Cactaceae, Caricaceae, Caryophyllaceae, Cannabaceae, Convolvulaceae, Chenopodiaceae, Elaeagnaceae, Geraniaceae, Gramineae, Juglandaceae, Lauraceae, Leguminosae, Linaceae, Cucurbitaceae, Cyperaceae, Euphorbiaceae, Fabaceae, Malvaceae, Nymphaeaceae, Papaveraceae, Rosaceae, Salicaceae, Solanaceae, Arecaceae, Iridaceae, Liliaceae, Orchidaceae, Gentianaceae, Labiaceae, Magnoliaceae, Ranunculaceae, Carifolaceae, Rubiaceae, Scrophulariaceae, Ericaceae, Polygonaceae, Violaceae, Juncaceae, Poaceae, perennial grass, fodder crops, vegetables and ornamentals.
- Especially preferred are plants selected from the groups of the families [0230.0.0.0] Apiaceae, Asteraceae, Brassicaceae, Cucurbitaceae, Fabaceae, Papaveraceae, 30 Rosaceae, Solanaceae, Liliaceae or Poaceae. Especially advantageous are, in particular, crop plants. Accordingly, an advantageous plant preferably belongs to the group of the genus peanut, oilseed rape, canola, sunflower, safflower, olive, sesame, hazelnut, almond, avocado, bay, pumpkin/squash, linseed, soya, pistachio, borage, maize, wheat, rye, oats, sorghum and millet, triticale, rice, barley, cassava, potato, 35 sugarbeet, fodder beet, egg plant, and perennial grasses and forage plants, oil palm. vegetables (brassicas, root vegetables, tuber vegetables, pod vegetables, fruiting vegetables, onion vegetables, leafy vegetables and stem vegetables), buckwheat, Jerusalem artichoke, broad bean, vetches, lentil, alfalfa, dwarf bean, lupin, clover and 40 lucerne.

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[0231.0.0.0] In order to introduce, into a plant, the nucleic acid molecule of the invention or used in the process according to the invention, it has proved advantageous first to transfer them into an intermediate host, for example a bacterium or a eukaryotic unicellular cell. The transformation into E. coli, which can be carried out in a manner known per se, for example by means of heat shock or electroporation, has proved itself expedient in this context. Thus, the transformed E. coli colonies can be analysed for their cloning efficiency. This can be carried out with the aid of a PCR. Here, not only the identity, but also the integrity, of the plasmid construct can be verified with the aid of a defined colony number by subjecting an aliquot of the colonies to said PCR. As a rule, universal primers which are derived from vector sequences are used for this purpose, it being possible, for example, for a forward primer to be arranged upstream of the start ATG and a reverse primer to be arranged downstream of the stop codon of the codogenic gene segment. The amplificates are separated by electrophoresis and assessed with regard to quantity and quality.

15 [0232.0.0.0] The nucleic acid constructs, which are optionally verified, are subsequently used for the transformation of the plants or other hosts, e.g. other eukaryotic cells or other prokaryotic cells. To this end, it may first be necessary to obtain the constructs from the intermediate host. For example, the constructs may be obtained as plasmids from bacterial hosts by a method similar to conventional plasmid isolation.

[0233.0.0.0] The nucleic acid molecule of the invention or used in the process according to the invention can also be introduced into modified viral vectors like baculovirus vectors for expression in insect cells or plant viral vectors like tobacco mosaic virus or potato virus X-based vectors. Approaches leading to the expression of proteins from the modified viral genome including the the nucleic acid molecule of the invention or used in the process according to the invention involve for example the inoculation of tobacco plants with infectious RNA transcribed in vitro from a cDNA copy of the recombinant viral genome. Another approach utilizes the transfection of whole plants from wounds inoculated with Agrobacterium tumefaciens containing cDNA copies of recombinant plus-sense RNA viruses. Different vectors and virus are known to the skilled worker for expression in different target eg. production plants.

[0234.0.0.0] A large number of methods for the transformation of plants are known. Since, in accordance with the invention, a stable integration of heterologous DNA into the genome of plants is advantageous, the T-DNA-mediated transformation has proved expedient in particular. For this purpose, it is first necessary to transform suitable vehicles, in particular agrobacteria, with a codogenic gene segment or the corresponding plasmid construct comprising the nucleic acid molecule of the invention. This can be carried out in a manner known per se. For example, said nucleic acid construct of the invention, or said expression construct or said plasmid construct, which has been generated in accordance with what has been detailed above, can be

transformed into competent agrobacteria by means of electroporation or heat shock. In principle, one must differentiate between the formation of cointegrated vectors on the one hand and the transformation with binary vectors on the other hand. In the case of the first alternative, the constructs, which comprise the codogenic gene segment or the nucleic acid molecule of the invention have no T-DNA sequences, but the formation of the cointegrated vectors or constructs takes place in the agrobacteria by homologous recombination of the construct with T-DNA. The T-DNA is present in the agrobacteria in the form of Ti or Ri plasmids in which exogenous DNA has expediently replaced the oncogenes. If binary vectors are used, they can be transferred to agrobacteria either by bacterial conjugation or by direct transfer. These agrobacteria expediently already comprise the vector bearing the vir genes (currently referred to as helper Ti(Ri) plasmid).

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[0235.0.0.0] One or more markers may expediently also be used together with the nucleic acid construct, or the vector of the invention and, if plants or plant cells shall be transformed together with the T-DNA, with the aid of which the isolation or selection of transformed organisms, such as agrobacteria or transformed plant cells, is possible. These marker genes enable the identification of a successful transfer of the nucleic acid molecules according to the invention via a series of different principles, for example via visual identification with the aid of fluorescence, luminescence or in the wavelength range of light which is discernible for the human eye, by a resistance to herbicides or antibiotics, via what are known as nutritive markers (auxotrophism markers) or antinutritive markers, via enzyme assays or via phytohormones. Examples of such markers which may be mentioned are GFP (= green fluorescent protein); the luciferin/luceferase system, the  $\beta$ -galactosidase with its colored substrates, for example X-Gal, the herbicide resistances to, for example, imidazolinone, glyphosate, phosphinothricin or sulfonylurea, the antibiotic resistances to, for example, bleomycin, hygromycin, streptomycin, kanamycin, tetracyclin, chloramphenicol, ampicillin, gentamycin, geneticin (G418), spectinomycin or blasticidin, to mention only a few, nutritive markers such as the utilization of mannose or xylose, or antinutritive markers such as the resistance to 2-deoxyglucose. This list is a small number of possible markers. The skilled worker is very familiar with such markers. Different markers are preferred, depending on the organism and the selection method.

[0236.0.0.0] As a rule, it is desired that the plant nucleic acid constructs are flanked by T-DNA at one or both sides of the codogenic gene segment. This is particularly useful when bacteria of the species Agrobacterium tumefaciens or Agrobacterium rhizogenes are used for the transformation. A method, which is preferred in accordance with the invention, is the transformation with the aid of Agrobacterium tumefaciens. However, biolistic methods may also be used advantageously for introducing the sequences in the process according to the invention, and the introduction by means of PEG is also possible. The transformed agrobacteria can be grown in the manner known per se and are thus available for the expedient transformation of the plants. The

plants or plant parts to be transformed are grown or provided in the customary manner. The transformed agrobacteria are subsequently allowed to act on the plants or plant parts until a sufficient transformation rate is reached. Allowing the agrobacteria to act on the plants or plant parts can take different forms. For example, a culture of morphogenic plant cells or tissue may be used. After the T-DNA transfer, antibiotics as a rule eliminate the bacteria, and the regeneration of plant tissue is induced. This is done in particular using suitable plant hormones in order to initially induce callus formation and then to promote shoot development.

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[0237.0.0.0] The transfer of foreign genes into the genome of a plant is called transformation. In doing this the methods described for the transformation and 10 regeneration of plants from plant tissues or plant cells are utilized for transient or stable transformation. An advantageous transformation method is the transformation in planta. To this end, it is possible, for example, to allow the agrobacteria to act on plant seeds or to inoculate the plant meristem with agrobacteria. It has proved particularly expedient in accordance with the invention to allow a suspension of transformed 15 agrobacteria to act on the intact plant or at least the flower primordia. The plant is subsequently grown on until the seeds of the treated plant are obtained (Clough and Bent, Plant J. (1998) 16, 735-743). To select transformed plants, the plant material obtained in the transformation is, as a rule, subjected to selective conditions so that transformed plants can be distinguished from untransformed plants. For example, the 20 seeds obtained in the above-described manner can be planted and, after an initial growing period, subjected to a suitable selection by spraying. A further possibility consists in growing the seeds, if appropriate after sterilization, on agar plates using a suitable selection agent so that only the transformed seeds can grow into plants. Further advantageous transformation methods, in particular for plants, are known to the 25 skilled worker and are described hereinbelow.

[0238.0.0.0] Further advantageous and suitable methods are protoplast transformation by poly (ethylene glycol)-induced DNA uptake, the "biolistic" method using the gene cannon - referred to as the particle bombardment method, electroporation, the incubation of dry embryos in DNA solution, microinjection and gene 30 transfer mediated by Agrobacterium. Said methods are described by way of example in B. Jenes et al., Techniques for Gene Transfer, in: Transgenic Plants, Vol. 1, Engineering and Utilization, eds. S.D. Kung and R. Wu, Academic Press (1993) 128-143 and in Potrykus Annu. Rev. Plant Physiol. Plant Molec. Biol. 42 (1991) 205-225). The nucleic acids or the construct to be expressed is preferably cloned into a vector, 35 which is suitable for transforming Agrobacterium tumefaciens, for example pBin19 (Bevan et al., Nucl. Acids Res. 12 (1984) 8711). Agrobacteria transformed by such a vector can then be used in known manner for the transformation of plants, in particular of crop plants such as by way of example tobacco plants, for example by bathing bruised leaves or chopped leaves in an agrobacterial solution and then culturing them 40 in suitable media. The transformation of plants by means of Agrobacterium

tumefaciens is described, for example, by Höfgen and Willmitzer in Nucl. Acid Res. (1988) 16, 9877 or is known inter alia from F.F. White, Vectors for Gene Transfer in Higher Plants; in Transgenic Plants, Vol. 1, Engineering and Utilization, eds. S.D. Kung and R. Wu, Academic Press, 1993, pp. 15-38.

- [0239.0.0.0] The abovementioned nucleic acid molecules can be cloned into the nucleic acid constructs or vectors according to the invention in combination together with further genes, or else different genes are introduced by transforming several nucleic acid constructs or vectors (including plasmids) into a host cell, advantageously into a plant cell or a microorgansims.
- [0240.0.0.0] In addition to the sequence mentioned in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 15 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 20 381, 383, 385, 387, 389, 391or 393 or its derivatives, it is advantageous additionally to express and/or mutate further genes in the organisms. Especially advantageously, additionally at least one further gene of the fine chemical biosynthetic pathway e.g. the amino acid biosynthetic pathway such as for L-tryptophane, L-isoleucine, L-leucine,
- 25 L-lysine, L-threonine and/or L-methionine to mention only a couple of them is expressed in the organisms such as plants or microorganisms. It is also possible that the regulation of the natural genes has been modified advantageously so that the gene and/or its gene product is no longer subject to the regulatory mechanisms which exist in the organisms. This leads to an increased synthesis of the fine chemicals e.g. the
- 35 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291,
- 40 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359,

361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 with genes which generally support or enhances to growth or yield of the target organismen, for example genes which lead to faster growth rate of microorganisms or genes which produces stress-, pathogen, or herbicide resistant plants.

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- [0241.0.0.0] In a further embodiment of the process of the invention, therefore, organisms are grown, in which there is simultaneous overexpression of at least one nucleic acid or one of the genes which code for proteins involved in the fine chemical metabolism e.g. the amino acid metabolism, in particular in amino acid synthesis.
- [0242.0.0.0] A further advantageous nucleic acid sequence which can be expressed in combination with the sequences used in the process and/or the abovementioned biosynthesis genes is the sequence of the ATP/ADP translocator as described in WO 01/20009. This ATP/ADP translocator leads to an increased synthesis of the essential amino acids lysine and/or methionine. Furthermore, an advantageous nucleic acid sequence coexpressed can be threonine adlolase and/or lysine decarboxylase as described in the state of the art.
  - [0243.0.0.0] In a further advantageous embodiment of the process of the invention, the organisms used in the process are those in which simultaneously at least one of the aforementioned genes or one of the aforementioned nucleic acids is mutated so that the activity of the corresponding proteins is influenced by metabolites to a smaller extent compared with the unmutated proteins, or not at all, and that in particular the production according to the invention of the fine chemical for example of the amino acids is not impaired, or so that their specific enzymatic activity is increased. Less influence means in this connection that the regulation of the enzymic activity is less by at least 10%, advantageously at least 20, 30 or 40%, particularly advantageously by at least 50, 60 or 70%, compared with the starting organism, and thus the activity of the enzyme is increased by these figures mentioned compared with the starting organism. An increase in the enzymatic activity means an enzymatic activity which is increased by at least 10%, advantageously at least 20, 30 or 40%, particularly advantageously by at least 50, 60 or 70%, compared with the starting organism. This leads to an increased productivity of the fine chemical.
    - [0244.0.0.0] In a further advantageous embodiment of the process of the invention, the organisms used in the process are those in which simultaneously the fine chemical degrading protein is attenuated, in particular by reducing the rate of expression of the corresponding gene.
    - [0245.0.0.0] In another embodiment of the process of the invention, the organisms used in the process are those in which simultaneously at least one of the aforementioned nucleic acids or of the aforementioned genes is mutated in such a way that the enzymatic activity of the corresponding protein is partially reduced or

completely blocked. A reduction in the enzymatic activity means an enzymatic activity, which is reduced by at least 10%, advantageously at least 20, 30 or 40%, particularly advantageously by at least 50, 60 or 70%, preferably more, compared with the starting organism.

[0246.0.0.0] If it is intended to transform the host cell, in particular the plant cell, with several constructs or vectors, the marker of a preceding transformation must be removed or a further marker employed in a following transformation. The markers can be removed from the host cell, in particular the plant cell, as described hereinbelow via methods with which the skilled worker is familiar. In particular plants without a marker, in particular without resistance to antibiotics, are an especially preferred embodiment of the present invention.

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[0247.0.0.0] In the process according to the invention, the nucleic acid sequences used in the process according to the invention are advantageously linked operably to one or more regulatory signals in order to increase gene expression. These regulatory sequences are intended to enable the specific expression of the genes and the expression of protein. Depending on the host organism for example plant or microorganism, this may mean, for example, that the gene is expressed and/or overexpressed after induction only, or that it is expressed and/or overexpressed constitutively. These regulatory sequences are, for example, sequences to which the inductors or repressors bind and which thus regulate the expression of the nucleic acid. In addition to these novel regulatory sequences, or instead of these sequences, the natural regulation of these sequences may still be present before the actual structural genes and, if appropriate, may have been genetically modified so that the natural regulation has been switched off and gene expression has been increased. However, the nucleic acid construct of the invention suitable as expression cassette (= expression construct = gene construct) can also be simpler in construction, that is to say no additional regulatory signals have been inserted before the nucleic acid sequence or its derivatives, and the natural promoter together with its regulation has not been removed. Instead, the natural regulatory sequence has been mutated in such a way that regulation no longer takes place and/or gene expression is increased. These modified promoters can also be introduced on their own before the natural gene in the form of part sequences (= promoter with parts of the nucleic acid sequences according to the invention) in order to increase the activity. Moreover, the gene construct can advantageously also comprise one or more of what are known as enhancer sequences in operable linkage with the promoter, and these enable an increased expression of the nucleic acid sequence. Also, it is possible to insert additional advantageous sequences at the 3' end of the DNA sequences, such as, for example, further regulatory elements or terminators.

[0248.0.0.0] The nucleic acid molecules, which encode proteins according to the invention and nucleic acid molecules, which encode other polypeptides may be present

in one nucleic acid construct or vector or in several ones. Advantageously, only one copy of the nucleic acid molecule of the invention or its encoding genes is present in the nucleic acid construct or vector. Several vectors or nucleic acid construct or vector can be expressed together in the host organism. The nucleic acid molecule or the nucleic acid construct or vector according to the invention can be inserted in a vector and be present in the cell in a free form. If a stable transformation is preferred, a vector is used, which is stably duplicated over several generations or which is else be inserted into the genome. In the case of plants, integration into the plastid genome or, in particular, into the nuclear genome may have taken place. For the insertion of more than one gene in the host genome the genes to be expressed are present together in one gene construct, for example in above-described vectors bearing a plurality of genes.

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[0249.0.0.0] As a rule, regulatory sequences for the expression rate of a gene are located upstream (5'), within, and/or downstream (3') relative to to the coding sequence of the nucleic acid molecule of the invention or another codogenic gene segment. They control in particular transcription and/or translation and/or the transcript stability. The expression level is dependent on the conjunction of further cellular regulatory systems, such as the protein biosynthesis and degradation systems of the cell.

[0250.0.0.0] Regulatory sequences include transcription and translation regulating sequences or signals, e.g. sequences located upstream (5'), which concern in particular the regulation of transcription or translation initiation, such as promoters or start codons, and sequences located downstream (3'), which concern in particular the regulation of transcription or translation termination and transcript stability, such as polyadenylation signals or stop codons. Regulatory sequences can also be present in transcribed coding regions as well in transcribed non-coding regions, e.g. in introns, as for example splicing sites. Promoters for the regulation of expression of the nucleic acid molecule according to the invention in a cell and which can be employed are, in principle, all those which are capable of stimulating the transcription of genes in the organisms in question, such as microorganisms or plants. Suitable promoters, which are functional in these organisms, are generally known. They may take the form of constitutive or inducible promoters. Suitable promoters can enable the developmentand/or tissue-specific expression in multi-celled eukaryotes; thus, leaf-, root-, flower-, seed-, stomata-, tuber- or fruit-specific promoters may advantageously be used in plants.

35 [0251.0.0.0] The regulatory sequences or factors can, as described above, have a positive effect on, the expression of the genes introduced, thus increasing their expression. Thus, an enhancement of the expression can advantageously take place at the transcriptional level by using strong transcription signals such as strong promoters and/or strong enhancers. In addition, enhancement of expression on the translational level is also possible, for example by introducing translation enhancer sequences, e.g.,

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the  $\Omega$  enhancer e.g. improving the ribosomal binding to the transcript, or by increasing the stability of the mRNA, e.g. by replacing the 3'UTR coding region by a region encoding a 3'UTR known as conferring an high stability of the transcript or by stabilization of the transcript through the elimination of transcript instability, so that the mRNA molecule is translated more often than the wild type. For example in plants AUrich elements (AREs) and DST (downstream) elements destabilized transcripts. Mutagenesis studies have demonstrated that residues within two of the conserved domains, the ATAGAT and the GTA regions, are necessary for instability function. Therefore removal or mutation of such elements would obviously lead to more stable transcripts, higher transcript rates and higher protein acitivity. Translation enhancers are also the "overdrive sequence", which comprises the tobacco mosaic virus 5'-untranslated leader sequence and which increases the protein/RNA ratio (Gallie et al., 1987, Nucl. Acids Research 15:8693-8711)

[0252.0.0.0] Enhancers are generally defined as cis active elements, which can stimulate gene transcription independent of position and orientation. Different enhancers have been identified in plants, which can either stimulate transcription constitutively or tissue or stimuli specific. Well known examples for constitutive enhancers are the enhancer from the 35S promoter (Odell et al., 1985, Nature 313:810-812) or the ocs enhancer (Fromm et al., 1989, Plant Cell 1: 977:984) Another examples are the G-Box motif tetramer which confers high-level constitutive expression in dicot and monocot plants (Ishige et al., 1999, Plant Journal, 18, 443-448) or the petE. a A/T-rich sequence which act as quantitative enhancers of gene expression in transgenic tobacco and potato plants (Sandhu et al., 1998; Plant Mol Biol. 37(5):885-96). Beside that, a large variety of cis-active elements have been described which contribute to specific expression pattern, like organ specific expression or induced expression in response to biotic or abiotic stress. Examples are elements, which provide pathogen or wound-induced expression (Rushton, 2002, Plant Cell, 14, 749-762) or guard cell-specific expression (Plesch, 2001, Plant Journal 28, 455-464).

[0253.0.0.0] Advantageous regulatory sequences for the expression of the nucleic acid molecule according to the invention in microorganisms are present for example in promoters such as the cos, tac, rha, trp, tet, trp-tet, lpp, lac, lpp-lac, lacl<sup>q-,</sup> T7, T5, T3, gal, trc, ara, SP6, λ-P<sub>R</sub> or λ-P<sub>L</sub> promoter, which are advantageously used in Gramnegative bacteria. Further advantageous regulatory sequences are present for example in the Gram-positive promoters amy, dnaK, xylS and SPO2, in the yeast or fungal promoters ADC1, MFα, AC, P-60, UASH, MCB, PHO, CYC1, GAPDH, TEF, rp28, ADH. Promoters, which are particularly advantageous, are constitutive, tissue or compartment specific and inducible promoters. In general, "promoter" is understood as meaning, in the present context, a regulatory sequence in a nucleic acid molecule, which mediates the expression of a coding sequence segment of a nucleic acid molecule. In general, the promoter is located upstream to the coding sequence

segment. Some elements, for example expression-enhancing elements such as enhancer may, however, also be located downstream or even in the transcribed region.

[0254.0.0.0] In principle, it is possible to use natural promoters together with their regulatory sequences, such as those mentioned above, for the novel process. It is also possible advantageously to use synthetic promoters, either additionally or alone, in particular when they mediate seed-specific expression such as described in, for example, WO 99/16890.

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[0255.0.0.0] The expression of the nucleic acid molecules used in the process may be desired alone or in combination with other genes or nucleic acids. Multiple nucleic acid molecules conferring the expression of advantageous genes can be introduced via the simultaneous transformation of several individual suitable nucleic acid constructs, i.e. expression constructs, or, preferably, by combining several expression cassettes on one construct. It is also possible to transform several vectors with in each case several expression cassettes stepwise into the recipient organisms.

[0256.0.0.0] As described above, the transcription of the genes introduced should advantageously be terminated by suitable terminators at the 3' end of the biosynthesis genes introduced (behind the stop codon). A terminator, which may be used for this purpose is, for example, the OCS1 terminator, the nos3 terminator or the 35S terminator. As is the case with the promoters, different terminator sequences should be used for each gene. Terminators, which are useful in microorganism, are for example the fimA terminator, txn terminator or trp terminator. Such terminators can be rhodependent or rho-independent.

[0257.0.0.0] Different plant promoters such as, for example, the USP, the LegB4-, the DC3 promoter or the ubiquitin promoter from parsley or other herein mentioned promoter and different terminators may advantageously be used in the nucleic acid construct.

[0258.0.0.0] In order to ensure the stable integration, into the transgenic plant, of nucleic acid molecules used in the process according to the invention in combination with further biosynthesis genes over a plurality of generations, each of the coding regions used in the process should be expressed under the control of its own, preferably unique, promoter since repeating sequence motifs may lead to recombination events or to silencing or, in plants, to instability of the T-DNA.

[0259.0.0.0] The nucleic acid construct is advantageously constructed in such a way that a promoter is followed by a suitable cleavage site for insertion of the nucleic acid to be expressed, advantageously in a polylinker, followed, if appropriate, by a terminator located behind the polylinker. If appropriate, this order is repeated several times so that several genes are combined in one construct and thus can be introduced into the transgenic plant in order to be expressed. The sequence is advantageously repeated

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up to three times. For the expression, the nucleic acid sequences are inserted via the suitable cleavage site, for example in the polylinker behind the promoter. It is advantageous for each nucleic acid sequence to have its own promoter and, if appropriate, its own terminator, as mentioned above. However, it is also possible to insert several nucleic acid sequences behind a promoter and, if appropriate, before a terminator if a polycistronic transcription is possible in the host or target cells. In this context, the insertion site, or the sequence of the nucleic acid molecules inserted, in the nucleic acid construct is not decisive, that is to say a nucleic acid molecule can be inserted in the first or last position in the cassette without this having a substantial effect on the expression. However, it is also possible to use only one promoter type in the construct. However, this may lead to undesired recombination events or silencing effects, as said.

[0260.0.0.0] Accordingly, in a preferred embodiment, the nucleic acid construct according to the invention confers expression of the nucleic acid molecule of the invention, and, optionally further genes, in a plant and comprises one or more plant regulatory elements. Said nucleic acid construct according to the invention advantageously encompasses a plant promoter or a plant terminator or a plant promoter and a plant terminator.

[0261.0.0.0] A "plant" promoter comprises regulatory elements, which mediate the expression of a coding sequence segment in plant cells. Accordingly, a plant promoter need not be of plant origin, but may originate from viruses or microorganisms, in particular for example from viruses which attack plant cells.

[0262.0.0.0] The plant promoter can also originates from a plant cell, e.g. from the plant, which is transformed with the nucleic acid construct or vector as described herein. This also applies to other "plant" regulatory signals, for example in "plant" terminators.

[0263.0.0.0] A nucleic acid construct suitable for plant expression preferably comprises regulatory elements which are capable of controlling the expression of genes in plant cells and which are operably linked so that each sequence can fulfill its function. Accordingly, the nucleic acid construct can also comprise transcription terminators. Examples for transcriptional termination are polyadenylation signals. Preferred polyadenylation signals are those which originate from Agrobacterium tumefaciens T-DNA, such as the gene 3 of the Ti plasmid pTiACH5, which is known as octopine synthase (Gielen et al., EMBO J. 3 (1984) 835 et seq.) or functional equivalents thereof, but all the other terminators which are functionally active in plants are also suitable.

[0264.0.0.0] The nucleic acid construct suitable for plant expression preferably also comprises other operably linked regulatory elements such as translation enhancers, for

example the overdrive sequence, which comprises the tobacco mosaic virus 5'-untranslated leader sequence, which increases the protein/RNA ratio (Gallie et al., 1987, Nucl. Acids Research 15:8693-8711).

- [0265.0.0.0] Other preferred sequences for use in operable linkage in gene expression constructs are targeting sequences, which are required for targeting the 5 gene product into specific cell compartments (for a review, see Kermode, Crit. Rev. Plant Sci. 15, 4 (1996) 285-423 and references cited therein), for example into the vacuole, the nucleus, all types of plastids, such as amyloplasts, chloroplasts, chromoplasts, the extracellular space, the mitochondria, the endoplasmic reticulum, 10 elaioplasts, peroxisomes, glycosomes, and other compartments of cells or extracellular. Sequences, which must be mentioned in this context are, in particular, the signal-peptide- or transit-peptide-encoding sequences which are known per se. For example, plastid-transit-peptide-encoding sequences enable the targeting of the expression product into the plastids of a plant cell. Targeting sequences are also known for eukaryotic and to a lower extent for prokaryotic organisms and can 15 advantageously be operable linked with the nucleic acid molecule of the present invention to achieve an expression in one of said compartments or extracellular.
- [0266.0.0.0] For expression in plants, the nucleic acid molecule must, as described above, be linked operably to or comprise a suitable promoter which expresses the gene at the right point in time and in a cell- or tissue-specific manner. Usable 20 promoters are constitutive promoters (Benfey et al., EMBO J. 8 (1989) 2195-2202), such as those which originate from plant viruses, such as 35S CAMV (Franck et al., Cell 21 (1980) 285-294), 19S CaMV (see also US 5352605 and WO 84/02913), 34S FMV (Sanger et al., Plant. Mol. Biol., 14, 1990: 433-443), the parsley ubiquitin promoter, or plant promoters such as the Rubisco small subunit promoter described in 25 US 4,962,028 or the plant promoters PRP1 [Ward et al., Plant. Mol. Biol. 22 (1993)], SSU, PGEL1, OCS [Leisner (1988) Proc Natl Acad Sci USA 85(5): 2553-2557], lib4, usp, mas [Comai (1990) Plant Mol Biol 15 (3):373-381], STLS1, ScBV (Schenk (1999) Plant Mol Biol 39(6):1221-1230), B33, SAD1 or SAD2 (flax promoters, Jain et al., Crop Science, 39 (6), 1999: 1696-1701) or nos [Shaw et al. (1984) Nucleic Acids Res. 30 12(20):7831-7846]. Stable, constitutive expression of the proteins according to the invention a plant can be advantageous. However, inducible expression of the polypeptide of the invention is advantageous, if a late expression before the harvest is of advantage, as metabolic manipulation may lead to a plant growth retardation.
- [0267.0.0.0] The expression of plant genes can also be facilitated as described above via a chemical inducible promoter (for a review, see Gatz 1997, Annu. Rev. Plant Physiol. Plant Mol. Biol., 48:89-108). Chemically inducible promoters are particularly suitable when it is desired to express the gene in a time-specific manner. Examples of such promoters are a salicylic acid inducible promoter (WO 95/19443), and abscisic acid-inducible promoter (EP 335 528), a tetracyclin-inducible promoter

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(Gatz et al. (1992) Plant J. 2, 397-404), a cyclohexanol- or ethanol-inducible promoter (WO 93/21334) or others as described herein.

[0268.0.0.0] Other suitable promoters are those which react to biotic or abiotic stress conditions, for example the pathogen-induced PRP1 gene promoter (Ward et al., Plant. Mol. Biol. 22 (1993) 361-366), the tomato heat-inducible hsp80 promoter (US 5,187,267), the potato chill-inducible alpha-amylase promoter (WO 96/12814) or the wound-inducible pinII promoter (EP-A-0 375 091) or others as described herein.

[0269.0.0.0] Preferred promoters are in particular those which bring about gene expression in tissues and organs in which the biosynthesis of fine chemical takes place, in seed cells, such as endosperm cells and cells of the developing embryo. Suitable promoters are the oilseed rape napin gene promoter (US 5,608,152), the Vicia faba USP promoter (Baeumlein et al., Mol Gen Genet, 1991, 225 (3):459-67), the Arabidopsis oleosin promoter (WO 98/45461), the Phaseolus vulgaris phaseolin promoter (US 5,504,200), the Brassica Bce4 promoter (WO 91/13980), the bean arc5 promoter, the carrot DcG3 promoter, or the Legumin B4 promoter (LeB4; Baeumlein et al., 1992, Plant Journal, 2 (2):233-9), and promoters which bring about the seedspecific expression in monocotyledonous plants such as maize, barley, wheat, rye, rice and the like. Advantageous seed-specific promoters are the sucrose binding protein promoter (WO 00/26388), the phaseolin promoter and the napin promoter. Suitable promoters which must be considered are the barley lpt2 or lpt1 gene promoter (WO 95/15389 and WO 95/23230), and the promoters described in WO 99/16890 (promoters from the barley hordein gene, the rice glutelin gene, the rice oryzin gene, the rice prolamin gene, the wheat gliadin gene, the wheat glutelin gene, the maize zein gene, the oat glutelin gene, the sorghum kasirin gene and the rye secalin gene). Further suitable promoters are Amy32b, Amy 6-6 and Aleurain [US 5,677,474], Bce4 (oilseed rape) [US 5,530,149], glycinin (soya) [EP 571 741], phosphoenolpyruvate carboxylase (soya) [JP 06/62870], ADR12-2 (soya) [WO 98/08962], isocitrate lyase (oilseed rape) [US 5,689,040] or α-amylase (barley) [EP 781 849]. Other promoters which are available for the expression of genes in plants are leaf-specific promoters such as those described in DE-A 19644478 or light-regulated promoters such as, for example, the pea petE promoter.

[0270.0.0.0] Further suitable plant promoters are the cytosolic FBPase promoter or the potato ST-LSI promoter (Stockhaus et al., EMBO J. 8, 1989, 2445), the Glycine max phosphoribosylpyrophosphate amidotransferase promoter (GenBank Accession No. U87999) or the node-specific promoter described in EP-A-0 249 676.

**[0271.0.0.0]** Other promoters, which are particularly suitable, are those, which bring about plastid-specific expression. Suitable promoters such as the viral RNA polymerase promoter are described in WO 95/16783 and WO 97/06250, and the Arabidopsis clpP promoter, which is described in WO 99/46394.

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[0272.0.0.0] Other promoters, which are used for the strong expression of heterologous sequences in as many tissues as possible, in particular also in leaves, are, in addition to several of the abovementioned viral and bacterial promoters, preferably, plant promoters of actin or ubiquitin genes such as, for example, the rice actin1 promoter. Further examples of constitutive plant promoters are the sugarbeet V-ATPase promoters (WO 01/14572). Examples of synthetic constitutive promoters are the Super promoter (WO 95/14098) and promoters derived from G-boxes (WO 94/12015). If appropriate, chemical inducible promoters may furthermore also be used, compare EP-A 388186, EP-A 335528, WO 97/06268.

10 [0273.0.0.0] As already mentioned herein, further regulatory sequences, which may be expedient, if appropriate, also include sequences, which target the transport and/or the localization of the expression products. Sequences, which must be mentioned in this context are, in particular, the signal-peptide- or transit-peptide-encoding sequences which are known per se. For example, plastid-transit-peptide-encoding sequences enable the targeting of the expression product into the plastids of a plant cell.

[0274.0.0.0] Preferred recipient plants are, as described above, in particular those plants, which can be transformed in a suitable manner. These include monocotyledonous and dicotyledonous plants. Plants which must be mentioned in particular are agriculturally useful plants such as cereals and grasses, for example Triticum spp., Zea mays, Hordeum vulgare, oats, Secale cereale, Oryza sativa, 20 Pennisetum glaucum, Sorghum bicolor, Triticale, Agrostis spp., Cenchrus ciliaris, Dactylis glomerata, Festuca arundinacea, Lolium spp., Medicago spp. and Saccharum spp., legumes and oil crops, for example Brassica juncea, Brassica napus, Glycine max, Arachis hypogaea, Gossypium hirsutum, Cicer arietinum, Helianthus annuus, Lens culinaris, Linum usitatissimum, Sinapis alba, Trifolium repens and Vicia 25 narbonensis, vegetables and fruits, for example bananas, grapes, Lycopersicon esculentum, asparagus, cabbage, watermelons, kiwi fruit, Solanum tuberosum, Beta vulgaris, cassava and chicory, trees, for example Coffea species, Citrus spp., Eucalyptus spp., Picea spp., Pinus spp. and Populus spp., medicinal plants and trees, and flowers.. 30

**[0275.0.0.0]** One embodiment of the present invention also relates to a method for generating a vector, which comprises the insertion, into a vector, of the nucleic acid molecule characterized herein, the nucleic acid molecule according to the invention or the expression cassette according to the invention. The vector can, for example, be introduced in to a cell, e.g. a microorganism or a plant cell, as described herein for the nucleic acid construct, or below under transformation or transfection or shown in the examples. A transient or stable transformation of the host or target cell is possible, however, a stable transformation is preferred. The vector according to the invention is preferably a vector, which is suitable for expressing the polypeptide according to the invention in a plant. The method can thus also encompass one or more steps for

integrating regulatory signals into the vector, in particular signals, which mediate the expression in microorganisms or plants.

[0276.0.0.0] Accordingly, the present invention also relates to a vector comprising the nucleic acid molecule characterized herein as part of a nucleic acid construct suitable for plant expression or the nucleic acid molecule according to the invention.

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[0277.0.0.0] The advantageous vectors of the invention comprise the nucleic acid molecules which encode proteins according to the invention, nucleic acid molecules which are used in the process, or nucleic acid construct suitable for plant expression comprising the nucleic acid molecules used, either alone or in combination with further genes such as the biosynthesis or regulatory genes of the fine chemical metabolism e.g. with the genes mentioned herein above. In accordance with the invention, the term "vector" refers to a nucleic acid molecule, which is capable of transporting another nucleic acid to which it is linked. One type of vector is a "plasmid", which means a circular double-stranded DNA loop into which additional DNA segments can be ligated. A further type of vector is a viral vector, it being possible to ligate additional nucleic acids segments into the viral genome. Certain vectors are capable of autonomous replication in a host cell into which they have been introduced (for example bacterial vectors with bacterial replication origin). Other preferred vectors are advantageously completely or partly integrated into the genome of a host cell when they are introduced into the host cell and thus replicate together with the host genome. Moreover, certain vectors are capable of controlling the expression of genes with which they are in operable linkage. In the present context, these vectors are referred to as "expression vectors". As mentioned above, they are capable of autonomous replication or may be integrated partly or completely into the host genome. Expression vectors, which are suitable for DNA recombination techniques usually, take the form of plasmids. In the present description, "plasmid" and "vector" can be used interchangeably since the plasmid is the most frequently used form of a vector. However, the invention is also intended to encompass these other forms of expression vectors, such as viral vectors, which exert similar functions. The term vector is furthermore also to encompass other vectors which are known to the skilled worker, such as phages, viruses such as SV40, CMV, TMV, transposons, IS elements, phasmids, phagemids, cosmids, and linear or circular DNA.

[0278.0.0.0] The recombinant expression vectors which are advantageously used in the process comprise the nucleic acid molecules according to the invention or the nucleic acid construct according to the invention in a form which is suitable for expressing, in a host cell, the nucleic acid molecules according to the invention or described herein. Accordingly, the the recombinant expression vectors comprise one or more regulatory signals selected on the basis of the host cells to be used for the expression, in operable linkage with the nucleic acid sequence to be expressed.

[0279.0.0.0] In a recombinant expression vector, "operable linkage" means that the nucleic acid molecule of interest is linked to the regulatory signals in such a way that expression of the nucleic acid molecule is possible: they are linked to one another in such a way that the two sequences fulfill the predicted function assigned to the sequence (for example in an in-vitro transcription/translation system, or in a host cell if the vector is introduced into the host cell).

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[0280.0.0.0] The term "regulatory sequence" is intended to comprise promoters, enhancers and other expression control elements (for example polyadenylation signalsThese regulatory sequences are described, for example, in Goeddel: Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, CA (1990), or see: Gruber and Crosby, in: Methods in Plant Molecular Biology and Biotechnolgy, CRC Press, Boca Raton, Florida, Ed.: Glick and Thompson, chapter 7, 89-108, including the references cited therein. Regulatory sequences encompass those, which control the constitutive expression of a nucleotide sequence in many types of host cells and those which control the direct expression of the nucleotide 15 sequence in specific host cells only, and under specific conditions. The skilled worker knows that the design of the expression vector may depend on factors such as the selection of the host cell to be transformed, the extent to which the desired protein is expressed, and the like. A preferred selection of regulatory sequences is described above, for example promoters, terminators, enhancers and the like. The term 20 regulatory sequence is to be considered as being encompassed by the term regulatory signal. Several advantageous regulatory sequences, in particular promoters and terminators are described above. In general, the regulatory sequences described as advantageous for nucleic acid construct suitable for expression are also applicable for 25 vectors.

[0281.0.0.0] The recombinant expression vectors used can be designed specifically for the expression, in prokaryotic and/or eukaryotic cells, of nucleic acid molecules used in the process. This is advantageous since intermediate steps of the vector construction are frequently carried out in microorganisms for the sake of simplicity. For example, the genes according to the invention and other genes can be expressed in bacterial cells, insect cells (using baculovirus expression vectors), yeast cells and other fungal cells [Romanos (1992), Yeast 8:423-488; van den Hondel, (1991), in: More Gene Manipulations in Fungi, J.W. Bennet & L.L. Lasure, Ed., pp. 396-428: Academic Press: San Diego; and van den Hondel, C.A.M.J.J. (1991), in: Applied Molecular Genetics of Fungi, Peberdy, J.F., et al., Ed., pp. 1-28, Cambridge University Press: Cambridge], algae [Falciatore et al., 1999, Marine Biotechnology.1, 3:239-251] using vectors and following a transformation method as described in WO 98/01572, and preferably in cells of multi-celled plants [see Schmidt, R. and Willmitzer, L. (1988) Plant Cell Rep.:583-586; Plant Molecular Biology and Biotechnology, C Press, Boca Raton, Florida, chapter 6/7, pp.71-119 (1993); F.F. White, in: Transgenic Plants, Bd. 1, Engineering and Utilization, Ed.: Kung and R. Wu, Academic Press (1993), 128-43;

Potrykus, Annu. Rev. Plant Physiol. Plant Molec. Biol. 42 (1991), 205-225 (and references cited therein)]. Suitable host cells are furthermore discussed in Goeddel, Gene Expression Technology: Methods in Enzymology 185, Academic Press, San Diego, CA (1990). As an alternative, the sequence of the recombinant expression vector can be transcribed and translated in vitro, for example using T7 promotor-regulatory sequences and T7 polymerase.

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[0282.0.0.0] Proteins can be expressed in prokaryotes using vectors comprising constitutive or inducible promoters, which control the expression of fusion proteins or nonfusion proteins. Typical fusion expression vectors are, inter alia, pGEX (Pharmacia Biotech Inc; Smith, D.B., and Johnson, K.S. (1988) Gene 67:31-40), pMAL (New 10 England Biolabs, Beverly, MA) and pRIT5 (Pharmacia, Piscataway, NJ), in which glutathione-S-transferase (GST), maltose-E-binding protein or protein A is fused with the recombinant target protein. Examples of suitable inducible nonfusion E. coli expression vectors are, inter alia, pTrc (Amann et al. (1988) Gene 69:301-315) and pET 11d [Studier et al., Gene Expression Technology: Methods in Enzymology 185, 15 Academic Press, San Diego, California (1990) 60-89]. The target gene expression of the pTrc vector is based on the transcription of a hybrid trp-lac fusion promoter by the host RNA polymerase. The target gene expression from the pET 11d vector is based on the transcription of a T7-gn10-lac fusion promoter, which is mediated by a coexpressed viral RNA polymerase (T7 gn1). This viral polymerase is provided by the 20 host strains BL21 (DE3) or HMS174 (DE3) by a resident λ-prophage, which harbors a T7 gn1 gene under the transcriptional control of the lacUV 5 promoter.

[0283.0.0.0] Other vectors which are suitable in prokaryotic organisms are known to the skilled worker; these vectors are for example in E. coli pLG338, pACYC184, the pBR series, such as pBR322, the pUC series such as pUC18 or pUC19, the M113mp series, pKC30, pRep4, pHS1, pHS2, pPLc236, pMBL24, pLG200, pUR290, pIN-III<sup>113</sup>-B1, λgt11 or pBdCl, in Streptomyces pIJ101, pIJ364, pIJ702 or pIJ361, in Bacillus pUB110, pC194 or pBD214, in Corynebacterium pSA77 or pAJ667.

[0284.0.0.0] In a further embodiment, the expression vector is a yeast expression vector. Examples of vectors for expression in the yeasts S. cerevisiae encompass pYeDesaturasec1 (Baldari et al. (1987) Embo J. 6:229-234), pMFa (Kurjan and Herskowitz (1982) Cell 30:933-943), pJRY88 (Schultz et al. (1987) Gene 54:113-123) and pYES2 (Invitrogen Corporation, San Diego, CA). Vectors and methods for the construction of vectors which are suitable for use in other fungi, such as the filamentous fungi, encompass those which are described in detail in: van den Hondel, C.A.M.J.J. [(1991), J.F. Peberdy, Ed., pp. 1-28, Cambridge University Press: Cambridge; or in: More Gene Manipulations in Fungi; J.W. Bennet & L.L. Lasure, Ed., pp. 396-428: Academic Press: San Diego]. Examples of other suitable yeast vectors are 2 m, pAG-1, YEp6, YEp13 or pEMBLYe23.

- [0285.0.0.0] Further vectors, which may be mentioned by way of example, are pALS1, pIL2 or pBB116 in fungi or pLGV23, pGHlac<sup>+</sup>, pBIN19, pAK2004 or pDH51 in plants.
- [0286.0.0.0] As an alternative, the nucleic acid sequences can be expressed in insect cells using baculovirus expression vectors. Baculovirus vectors which are available for expressing proteins in cultured insect cells (for example Sf9 cells) encompass the pAc series (Smith et al. (1983) Mol. Cell Biol. 3:2156-2165) and the pVL series (Lucklow and Summers (1989) Virology 170:31-39).
- [0287.0.0.0] The abovementioned vectors are only a small overview of potentially suitable vectors. Further plasmids are known to the skilled worker and are described, for example, in: Cloning Vectors (Ed. Pouwels, P.H., et al., Elsevier, Amsterdam-New York-Oxford, 1985, ISBN 0 444 904018). Further suitable expression systems for prokaryotic and eukaryotic cells, see the chapters 16 and 17 by Sambrook, J., Fritsch, E.F., and Maniatis, T., Molecular Cloning: A Laboratory Manual, 2nd Edition, Cold Spring Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989.
  - [0288.0.0.0] Accordingly, one embodiment of the invention relates to a vector where the nucleic acid molecule according to the invention is linked operably to regulatory sequences which permit the expression in a prokaryotic or eukaryotic or in a prokaryotic and eukaryotic host.
  - [0289.0.0.0] Accordingly, one embodiment of the invention relates to a host cell, which has been transformed stably or transiently with the vector according to the invention or the nucleic acid molecule according to the invention or the nucleic acid construct according to the invention.

[0290.0.0.0] Depending on the host organism, the organisms used in the process 25 according to the invention are cultured or grown in a manner with which the skilled worker is familiar. As a rule, microorganisms are grown in a liquid medium comprising a carbon source, usually in the form of sugars, a nitrogen source, usually in the form of organic nitrogen sources such as yeast extract or salts such as ammonium sulfate, trace elements such as iron salts, manganese salts, magnesium salts, and, if 30 appropriate, vitamins, at temperatures between 0°C and 100°C, preferably between 10°C and 60°C, while passing in oxygen. In the event the microorganism is anaerobe, no oxygen is blown through the culture medium. The pH value of the liquid nutrient medium may be kept constant, that is to say regulated during the culturing phase, or not. The organisms may be cultured batchwise, semibatchwise or continuously. 35 Nutrients may be provided at the beginning of the fermentation or fed in semicontinuously or continuously.

- [0291.0.0.0] The fine chemical produced can be isolated from the organism by methods with which the skilled worker is familiar. For example via extraction, salt precipitation and/or ion-exchange chromatography etc. To this end, the organisms may be disrupted beforehand. The process according to the invention can be conducted batchwise, semibatchwise or continuously. A summary of known culture and isolation techniques can be found in the textbook by Chmiel [Bioprozeßtechnik 1, Einführung in die Bioverfahrenstechnik (Gustav Fischer Verlag, Stuttgart, 1991)], Demain et al. (Industrial Microbiology and Biotechnology, second edition, ASM Press, Washington, D.C., 1999, ISBN 1-55581-128-0] or in the textbook by Storhas [Bioreaktoren und periphere Einrichtungen (Vieweg Verlag, Braunschweig/Wiesbaden, 1994)].
- [0292.0.0.0] In one embodiment, the present invention relates to a polypeptide encoded by the nucleic acid molecule according to the present invention, preferably conferring an increase in the fine chemical content in an organism or cell after increasing the expression or activity.
- 15 **[0293.0.0.0]** The present invention also relates to a process for the production of a polypeptide according to the present invention, the polypeptide being expressed in a host cell according to the invention, preferably in a microorganism or a transgenic plant cell.
- [0294.0.0.0] In one embodiment, the nucleic acid molecule used in the process for the production of the polypeptide is derived from a microorganism, preferably from a prokaryotic or protozoic cell with a eukaryotic organism as host cell. E.g., in one embodiment the polypeptide is produced in a plant cell or plant with a nucleic acid molecule derived from a prokaryote or a fungus or an alga or another microorganismus but not from plant.
- [0295.0.0.0] The skilled worker knows that protein and DNA expressed in different organisms differ in many respects and properties, e.g. DNA modulation and imprinting, such as methylation or post-translational modification, as for example glucosylation, phosphorylation, acetylation, myristoylation, ADP-ribosylation, farnesylation, carboxylation, sulfation, ubiquination, etc. though having the same coding sequence.
   Preferably, the cellular expression control of the corresponding protein differs accordingly in the control mechanisms controlling the activity and expression of an endogenous protein or another eukaryotic protein. One major difference between proteins expressed in prokaryotic or eukaryotic organisms is the amount and pattern of glycosylation. For example in E. coli there are no glycosylated proteins. Proteins
   expressed in yeasts have high mannose content in the glycosylated proteins, whereas in plants the glycosylation pattern is complex.
  - [0296.0.0.0] The polypeptide of the present invention is preferably produced by recombinant DNA techniques. For example, a nucleic acid molecule encoding the

protein is cloned into a vector (as described above), the vector is introduced into a host cell (as described above) and said polypeptide is expressed in the host cell. Said polypeptide can then be isolated from the cells by an appropriate purification scheme using standard protein purification techniques. Alternative to recombinant expression, the polypeptide or peptide of the present invention can be synthesized chemically using standard peptide synthesis techniques.

[0297.0.0.0] Moreover, native polypeptides conferring the increase of the fine chemical in an organism or part thereof can be isolated from cells (e.g., endothelial cells), for example using the antibody of the present invention as described below, in particular, an anti-YNL090W protein antibody or an antibody against polypeptides as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 15 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 20 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394, which can be produced by standard techniques utilizing the polypeptid of the present invention or fragment thereof, i.e., the polypeptide of this invention. Preferred are monoclonal antibodies.

[0298.0.0.0] In one embodiment, the present invention relates to a polypeptide having the amino acid sequence encoded by a nucleic acid molecule of the invention or obtainable by a process of the invention. Said polypeptide confers preferably the aforementioned activity, in particular, the polypeptide confers the increase of the fine chemical in a cell or an organsim or a part thereof after increasing the cellular activity, e.g. by increasing the expression or the specific activity of the polypeptide.

[0299.0.0.0] In one embodiment, the present invention relates to a polypeptide having the sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320,

322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or as coded by the nucleic acid molecule as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393or functional homologues thereof.

[0300.0.0.0] In one advantageous embodiment, in the method of the present invention the activity of a polypeptide is increased comprising or consisting of the consensus sequence as depicted in SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 397, SEQ ID NO: 398, SEQ ID NO: 399 and/or SEQ ID NO: 400 and in one another embodiment, the present invention relates to a polypeptide comprising or consisting of the consensus sequence as depicted in SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 397, SEQ ID NO: 398, SEQ ID NO: 399 and/or SEQ ID NO: 400 whereby 20 or less, preferably 15 or 10, preferably 9, 8, 7, or 6, more preferred 5 or 4, even more preferred 3, even more preferred 2, even more preferred 1, most preferred 0 of the amino acids positions indicated can be replaced by any amino acid.

[0301.0.0.0] In one embodiment not more than 15%, preferably 10%, even more preferred 5%, 4%, 3%, or 2%, most preferred 1% or 0% of the amino acid position indicated by a letter are/is replaced another amino acid.

[0302.0.0.0] In one embodiment 20 or less, preferably 15 or 10, preferably 9, 8, 7, or 6, more preferred 5 or 4, even more preferred 3, even more preferred 2, even more preferred 1, most preferred 0 amino acids are inserted into the consensus sequence.

[0303.0.0.0] The consensus sequences of specified domains were derived from a multiple alignment of all sequences. The consensus sequences are disclosed under SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 397, SEQ ID NO: 398, SEQ ID NO: 399 and/or SEQ ID NO: 400. The letters represent the three letter amino acid code and indicate that the amino acids are conserved in all aligned proteins. The letter Xaa stands for amino acids, which are not conserved in all sequences. In some cases of the sequences as

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depicted in SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 397, SEQ ID NO: 398, SEQ ID NO: 399 and/or SEQ ID NO: 400 preferred amino acids are mentioned in the sequence protocol in others all natural amino acids are possible. Figur 1 shows an alignment with part of the sequences in the one letter amino acid code. The conserved sequences are framed.

The alignment was performed either with the Software AlignX (sept [0304.0.0.0] 25, 2002) a component of Vector NTI Suite 8.0 , InforMax™,Invitrogen™ life science software, U.S. Main Office, 7305 Executive Way, Frederick, MD 21704, USA with the following settings: For pairwise alignments: gap opening penality: 10,0; gap extension 10 penality 0,1. For multiple alignments: Gap opening penalty: 10,0; Gap extension penalty: 0,1; Gap separation penalty range: 8; Residue substitution matrix: blosum62; Hydrophilic residues: GPSNDQEKR; Transition weighting: 0,5; Consensus calculation options: Residue fraction for consensus: 1 or preferably the percent sequence identity between two nucleic acid or polypeptide sequences was determined 15 using the Vector NTI 6.0 (PC) software package (InforMax, 7600 Wisconsin Ave., Bethesda, MD 20814). A gap opening penalty of 15 and a gap extension penalty of 6.66 are used for determining the percent identity of two nucleic acids. A gap opening penalty of 10 and a gap extension penalty of 0.1 are used for determining the percent identity of two polypeptides. All other parameters are set at the default settings. For 20 purposes of a multiple alignment (Clustal W algorithm), the gap opening penalty is 10, and the gap extension penalty is 0.05 with blosum62 matrix.

In one advantageous embodiment, the method of the present invention comprises the increasing of a polypeptide comprising or consisting of plant or microorganism specific consensus sequences, 25 In one embodiment, said polypeptide of the invention distinguishes over the sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 30 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 35 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 by one or more amino acids. In one embodiment, polypeptide distinguishes form the sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 40

84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120,

122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 by more than 5, 6, 7, 8 or 9 amino acids, preferably by more than 10, 15, 20, 25 or 30 amino acids, evenmore preferred are more than 40, 50, or 60 amino acids and, 10 preferably, the sequence of the polypeptide of the invention distinguishes from the sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 15 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 20 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 by not more than 80% or 70% of the amino acids, preferably not more than 60% or 50%, more preferred not more than 40% or 30%, even more preferred not more than 25 20% or 10%. In an other embodiment, said polypeptide of the invention does not consist of the sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148<u>.</u> 30 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 35 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394.

[0306.0.0.0] In one embodiment, the polypeptide of the invention comprises any one of the sequences not known to the public before. In one embodiment, the polypeptide of the invention orginates from a non-plant cell, in particular from a microorganism, and was expressed in a plant cell. In one embodiment, the present invention relates to a

polypeptide encoded by the nucleic acid molecule of the invention or used in the process of the invention for which an activity has not been described yet.

[0307.0.0.0] In one embodiment, the invention relates to polypeptide conferring an increase in the fine chemical in an organism or part being encoded by the nucleic acid molecule of the invention or used in the process of the invention and having a 5 sequence which distinguishes from the sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 10 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 15 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 by one or more amino acids. In an other embodiment, said polypeptide of the invention does not consist of the sequence as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 20 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 25 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394. In a further embodiment, said polypeptide of the present invention is less than 100%, 30 99,999%, 99,99%, 99,9% or 99% identical. In one embodiment, said polypeptide does not consist of the sequence encoded by the nucleic acid molecules as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 35 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 40 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337,

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339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393.

[0308.0.0.0] In one embodiment, the present invention relates to a polypeptide having the biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60. 5 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172. 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 10 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240. 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394and which distinguishes over the 15 aforementioned sequences by one or more amino acids, preferably by more than 5, 6, 7, 8 or 9 amino acids, preferably by more than 10, 15, 20, 25 or 30 amino acids. evenmore preferred are more than 40, 50, or 60 amino acids but even more preferred by less than 70% of the amino acids, more preferred by less than 50%, even more preferred my less than 30% or 25%, more preferred are 20% or 15%, even more 20 preferred are less than 10%.

[0309.0.0.0] The terms "protein" and "polypeptide" used in this application are interchangeable. "Polypeptide" refers to a polymer of amino acids (amino acid sequence) and does not refer to a specific length of the molecule. Thus peptides and oligopeptides are included within the definition of polypeptide. This term does also refer to or include post-translational modifications of the polypeptide, for example, glycosylations, acetylations, phosphorylations and the like. Included within the definition are, for example, polypeptides containing one or more analogs of an amino acid (including, for example, unnatural amino acids, etc.), polypeptides with substituted linkages, as well as other modifications known in the art, both naturally occurring and non-naturally occurring.

[0310.0.0.0] Preferably, the polypeptide is isolated. An "isolated" or "purified" protein or nucleic acid molecule or biologically active portion thereof is substantially free of cellular material when produced by recombinant DNA techniques or chemical precursors or other chemicals when chemically synthesized.

[0311.0.0.0] The language "substantially free of cellular material" includes preparations of the polypeptide of the invention in which the protein is separated from cellular components of the cells in which it is naturally or recombinantly produced. In one embodiment, the language "substantially free of cellular material" includes

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preparations having less than about 30% (by dry weight) of "contaminating protein", more preferably less than about 20% of "contaminating protein", still more preferably less than about 10% of "contaminating protein", and most preferably less than about 5% "contaminating protein". The term "Contaminating protein" relates to polypeptides, which are not polypeptides of the present invention. When the polypeptide of the present invention or biologically active portion thereof is recombinantly produced, it is also preferably substantially free of culture medium, i.e., culture medium represents less than about 20%, more preferably less than about 10%, and most preferably less than about 5% of the volume of the protein preparation. The language "substantially free of chemical precursors or other chemicals" includes preparations in which the polypeptide of the present invention is separated from chemical precursors or other chemicals, which are involved in the synthesis of the protein. The language "substantially free of chemical precursors or other chemicals" includes preparations having less than about 30% (by dry weight) of chemical precursors or non-polypeptide of the inventionchemicals, more preferably less than about 20% chemical precursors or non-polypeptide of the inventionchemicals, still more preferably less than about 10% chemical precursors or non-polypeptide of the invention-chemicals, and most preferably less than about 5% chemical precursors or non- polypeptide of the invention-chemicals. In preferred embodiments, isolated proteins or biologically active portions thereof lack contaminating proteins from the same organism from which the polypeptide of the present invention is derived. Typically, such proteins are produced by recombinant techniques.

[0312.0.0.0] A polypeptide of the invention can participate in the process of the present invention. The polypeptide or a portion thereof comprises preferably an amino acid sequence which is sufficiently homologous to an amino acid sequence as depicted 25 in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 30 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 35 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 such that the protein or portion thereof maintains the ability to confer the activity of the present invention. The portion of the protein is preferably a biologically active portion as described herein. Preferably, the polypeptide used in the processof the invention has an amino acid sequence identical as shown in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 40 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78,

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80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394.

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[0313.0.0.0] Further, the polypeptide can have an amino acid sequence which is encoded by a nucleotide sequence which hybridizes, preferably hybridizes under stringent conditions as described above, to a nucleotide sequence of the nucleic acid molecule of the present invention. Accordingly, the polypeptide has an amino acid sequence which is encoded by a nucleotide sequence that is at least about 35%, 40%, 15 45%, 50%, 55%, 60%, 65% or 70%, preferably at least about 75%, 80%, 85% or 90, and more preferably at least about 91%, 92%, 93%, 94% or 95%, and even more preferably at least about 96%, 97%, 98%, 99% or more homologous to one of the amino acid sequences of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 20 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 25 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 268, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394. The preferred polypeptide of the present invention preferably possesses at least 30 one of the activities according to the invention and described herein. A preferred polypeptide of the present invention includes an amino acid sequence encoded by a nucleotide sequence which hybridizes, preferably hybridizes under stringent conditions, to a nucleotide sequence of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 35 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289,

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291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 or which is homologous thereto, as defined above.

[0314.0.0.0] Accordingly the polypeptide of the present invention can vary from SEQ 5 ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 10 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 15 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 in amino acid sequence due to natural variation or mutagenesis, as described in detail herein. Accordingly, the polypeptide comprise an amino acid sequence which is at least about 35%, 40%, 45%, 50%, 55%, 60%, 65% or 70%, preferably at least about 75%, 80%, 85% or 90, and more preferably at least about 91%, 92%, 93%, 94% or 95%, and most preferably at 20 least about 96%, 97%, 98%, 99% or more homologous to an entire amino acid sequence of SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 25 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 30 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394.

[0315.0.0.0] For the comparison of amino acid sequences the same algorithms as described above or nucleic acid sequences can be used. Results of high quality are reached by using the algorithm of Needleman and Wunsch or Smith and Waterman. Therefore programs based on said algorithms are preferred. Advantageously the comparisons of sequences can be done with the program PileUp (J. Mol. Evolution., 25, 351-360, 1987, Higgins et al., CABIOS, 5 1989: 151–153) or preferably with the programs Gap and BestFit, which are respectively based on the algorithms of Needleman and Wunsch [J. Mol. Biol. 48; 443-453 (1970)] and Smith and Waterman [Adv. Appl. Math. 2; 482-489 (1981)]. Both programs are part of the GCG software-

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package [Genetics Computer Group, 575 Science Drive, Madison, Wisconsin, USA 53711 (1991); Altschul et al. (1997) Nucleic Acids Res. 25:3389 et seq.]. Therefore preferably the calculations to determine the perentages of sequence homology are done with the program Gap over the whole range of the sequences. The following standard adjustments for the comparison of amino acid sequences were used: gap weight: 8, length weight: 2, average match: 2.912, average mismatch: -2.003.

Biologically active portions of an polypeptide of the present invention include peptides comprising amino acid sequences derived from the amino acid sequence of the polypeptide of the present invention or used in the process of the present invention, e.g., the amino acid sequence shown in SEQ ID NO: 2, 4, 6, 8, 10. 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or the amino acid sequence of a protein homologous thereto, which include fewer amino acids than a full length polypeptide of the present invention or used in the process of the present invention or the full length protein which is homologous to an polypeptide of the present invention or used in the process of the present invention depicted herein, and exhibit at least one activity of polypeptide of the present invention or used in the process of the present invention.

[0317.0.0.0] Typically, biologically (or immunologically) active portions i.e. peptides, e.g., peptides which are, for example, 5, 10, 15, 20, 30, 35, 36, 37, 38; 39, 40, 50, 100 or more amino acids in length comprise a domain or motif with at least one activity or epitope of a polypeptide of the present invention or used in the process of the present invention. Moreover, other biologically active portions, in which other regions of the polypeptide are deleted, can be prepared by recombinant techniques and evaluated for one or more of the activities described herein.

[0318.0.0.0] Manipulation of the nucleic acid molecule of the invention may result in the production of proteins having the biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194,

196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 and having differences from said aforementioned wild-type proteins. These proteins may be improved in efficiency or activity, may be present in greater numbers in the cell than is usual, or may be decreased in efficiency or activity in relation to the wild type protein.

- [0319.0.0.0] Any mutagenesis strategies for the polypeptide of the present invention or the polypeptide used in the process of the present invention to result in increasing said activity are not meant to be limiting; variations on these strategies will be readily apparent to one skilled in the art. Using such strategies, and incorporating the mechanisms disclosed herein, the nucleic acid molecule and polypeptide of the invention may be utilized to generate plants or parts thereof, expressing wildtype proteins of the invention or mutated protein encoding nucleic acid molecules and polypeptide molecules of the invention such that the yield, production, and/or efficiency of production of a desired compound is improved.
- [0320.0.0.0] This desired compound may be any natural product of plants, which includes the final products of biosynthesis pathways and intermediates of naturally-occurring metabolic pathways, as well as molecules which do not naturally occur in the metabolism of said cells, but which are produced by a said cells of the invention. Preferrably, the compound is a composition of amino acids or a recovered amino acid, in particular, the fine chemical, free or in protein-bound form.
- 25 [0321.0.0.0] The invention also provides chimeric or fusion proteins.
  - [0322.0.0.0] As used herein, an "chimeric protein" or "fusion protein" comprises an polypeptide operatively linked to a polypeptide which does not confer above-mentioned activity, in particulare, which does not confer an increase of content of the fine chemical in a cell or an organism or a part thereof, if its activity is increased.
- [0323.0.0.0] In one embodiment, a protein (= polypeptide)" having the biological activity represented by a protein as depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282,

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[0324.0.0.0] Within the fusion protein, the term "operatively linked" is intended to indicate that the polypeptide of the invention or a polypeptide used in the process of the invention and the "other polypeptide" or a part thereof are fused to each other so that both sequences fulfil the proposed function addicted to the sequence used. The "other polypeptide" can be fused to the N-terminus or C-terminus of the polypeptide of the invention or used in the process of the invention. For example, in one embodiment the fusion protein is a GST-LMRP fusion protein in which the sequences of the polypeptide of the invention or the polypeptide used in the process of the invention are fused to the C-terminus of the GST sequences. Such fusion proteins can facilitate the purification of recombinant polypeptides of the invention or a poylpeptide usefull in the process of the invention.

[0325.0.0.0] In another embodiment, the fusion protein is a polypeptide of the invention or a polypeptide used in the process of the invention containing a heterologous signal sequence at its N-terminus. In certain host cells (e.g., mammalian host cells), expression and/or secretion of a polypeptide of the invention or a polypeptide used in the process of the invention can be increased through use of a heterologous signal sequence. As already mentioned above, targeting sequences, are required for targeting the gene product into specific cell compartment (for a review, see Kermode, Crit. Rev. Plant Sci. 15, 4 (1996) 285-423 and references cited therein), for

example into the vacuole, the nucleus, all types of plastids, such as amyloplasts, chloroplasts, chromoplasts, the extracellular space, the mitochondria, the endoplasmic reticulum, elaioplasts, peroxisomes, glycosomes, and other compartments of cells or extracellular. Sequences, which must be mentioned in this context are, in particular, the signal-peptide- or transit-peptide-encoding sequences which are known per se. For example, plastid-transit-peptide-encoding sequences enable the targeting of the expression product into the plastids of a plant cell. Targeting sequences are also known for eukaryotic and to a lower extent for prokaryotic organisms and can advantageously be operable linked with the nucleic acid molecule of the present invention to achieve an expression in one of said compartments or extracellular.

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[0326.0.0.0] Preferably, a chimeric or fusion protein of the invention is produced by standard recombinant DNA techniques. For example, DNA fragments coding for the different polypeptide sequences are ligated together in-frame in accordance with conventional techniques, for example by employing blunt-ended or stagger-ended termini for ligation, restriction enzyme digestion to provide for appropriate termini, filling-in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesirable joining, and enzymatic ligation. The fusion gene can be synthesized by conventional techniques including automated DNA synthesizers. Alternatively, PCR amplification of gene fragments can be carried out using anchor primers, which give rise to complementary overhangs between two consecutive gene fragments which can subsequently be annealed and reamplified to generate a chimeric gene sequence (see, for example, Current Protocols in Molecular Biology, eds. Ausubel et al. John Wiley & Sons: 1992). Moreover, many expression vectors are commercially available that already encode a fusion moiety (e.g., a GST polypeptide). The nucleic acid molecule of the invention can be cloned into such an expression vector such that the fusion moiety is linked in-frame to the encoded protein.

[0327.0.0.0] Furthermore, folding simulations and computer redesign of structural motifs of the protein of the invention can be performed using appropriate computer programs (Olszewski, Proteins 25 (1996), 286-299; Hoffman, Comput. Appl. Biosci. 11 (1995), 675-679). Computer modeling of protein folding can be used for the conformational and energetic analysis of detailed peptide and protein models (Monge, J. Mol. Biol. 247 (1995), 995-1012; Renouf, Adv. Exp. Med. Biol. 376 (1995), 37-45). The appropriate programs can be used for the identification of interactive sites the polypeptide of the invention or polypeptides used in the process of the invention and its substrates or binding factors or other interacting proteins by computer assistant searches for complementary peptide sequences (Fassina, Immunomethods (1994), 114-120). Further appropriate computer systems for the design of protein and peptides are described in the prior art, for example in Berry, Biochem. Soc. Trans. 22 (1994), 1033-1036; Wodak, Ann. N. Y. Acad. Sci. 501 (1987), 1-13; Pabo, Biochemistry 25 (1986), 5987-5991. The results obtained from the above-described computer analysis can be used for, e.g., the preparation of peptidomimetics of the protein of the invention

or fragments thereof. Such pseudopeptide analogues of the, natural amino acid sequence of the protein may very efficiently mimic the parent protein (Benkirane, J. Biol. Chem. 271 (1996), 33218-33224). For example, incorporation of easily available achiral Q-amino acid residues into a protein of the invention or a fragment thereof results in the substitution of amide bonds by polymethylene units of an aliphatic chain, thereby providing a convenient strategy for constructing a peptidomimetic (Banerjee, Biopolymers 39 (1996), 769-777).

[0328.0.0.0] Superactive peptidomimetic analogues of small peptide hormones in other systems are described in the prior art (Zhang, Biochem. Biophys. Res. Commun.
224 (1996), 327-331). Appropriate peptidomimetics of the protein of the present invention can also be identified by the synthesis of peptidomimetic combinatorial libraries through successive amide alkylation and testing the resulting compounds, e.g., for their binding and immunological properties. Methods for the generation and use of peptidomimetic combinatorial libraries are described in the prior art, for example in
Ostresh, Methods in Enzymology 267 (1996), 220-234 and Dorner, Bioorg. Med. Chem. 4 (1996), 709-715.

[0329.0.0.0] Furthermore, a three-dimensional and/or crystallographic structure of the protein of the invention can be used for the design of peptidomimetic inhibitors of the biological activity of the protein of the invention (Rose, Biochemistry 35 (1996), 12933-12944; Rutenber, Bioorg. Med. Chem. 4 (1996), 1545-1558).

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[0330.0.0.0] Furthermore, a three-dimensional and/or crystallographic structure of the protein of the invention and the identification of interactive sites the polypeptide of the invention and its substrates or binding factors can be used for design of mutants with modulated binding or turn over activities. For example, the active center of the polypeptide of the present invention can be modelled and amino acid residues participating in the catalytic reaction can be modulated to increase or decrease the binding of the substrate to activate or improve the polypeptide. The identification of the active center and the amino acids involved in the catalytic reaction facilitates the screening for mutants having an increased activity.

[0331.0.0.0] One embodiment of the invention also relates to an antibody, which binds specifically to the polypeptide according to the invention or parts, i.e. specific fragments or epitopes of such a protein.

[0332.0.0.0] The antibodies of the invention can be used to identify and isolate the polypeptide according to the invention and encoding genes in any organism, preferably plants, prepared in plants described herein. These antibodies can be monoclonal antibodies, polyclonal antibodies or synthetic antibodies as well as fragments of antibodies, such as Fab, Fv or scFv fragments etc. Monoclonal antibodies can be prepared, for example, by the techniques as originally described in Köhler and Milstein,

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Nature 256 (1975), 495, and Galfr6, Meth. Enzymol. 73 (1981), 3, which comprise the fusion of mouse myeloma cells to spleen cells derived from immunized mammals.

[0333.0.0.0] Furthermore, antibodies or fragments thereof to the aforementioned peptides can be obtained by using methods, which are described, e.g., in Harlow and Lane "Antibodies, A Laboratory Manual", CSH Press, Cold Spring Harbor, 1988. These antibodies can be used, for example, for the immunoprecipitation and immunolocalization of proteins according to the invention as well as for the monitoring of the synthesis of such proteins, for example, in recombinant organisms, and for the identification of compounds interacting with the protein according to the invention. For example, surface plasmon resonance as employed in the BIAcore system can be used to increase the efficiency of phage antibodies selections, yielding a high increment of affinity from a single library of phage antibodies, which bind to an epitope of the protein of the invention (Schier, Human Antibodies Hybridomas 7 (1996), 97-105; Malmborg, J. Immunol. Methods 183 (1995), 7-13). In many cases, the binding phenomena of antibodies to antigens are equivalent to other ligand/anti-ligand binding.

[0334.0.0.0] In one embodiment, the present invention relates to an antisense nucleic acid molecule comprising the complementary sequence of the nucleic acid molecule of the present invention.

[0335.0.0.0] Methods to modify the expression levels and/or the activity are known to persons skilled in the art and include for instance overexpression, co-suppression, the use of ribozymes, sense and anti-sense strategies or other gene silencing approaches like RNA interference (RNAi) or promoter methylation."Sense strand" refers to the strand of a double-stranded DNA molecule that is homologous to an mRNA transcript thereof. The "anti-sense strand" contains an inverted sequence, which is complementary to that of the "sense strand".

In addition the expression levels and/or the activity can be modified by the introduction of mutations in the regulatory or coding regions of the nucleic acids of the invention. Furthermore antibodies can be expressed which specifically binds to a polypeptide of interest and thereby blocks it acitivity. The protein-binding factors can, for example, also be aptamers [Famulok M and Mayer G (1999) Curr. Top Microbiol. Immunol. 243: 123-36] or antibodies or antibody fragments or single-chain antibodies. Obtaining these factors has been described, and the skilled worker is familiar therewith. For example, a cytoplasmic scFv antibody has been employed for modulating activity of the phytochrome A protein in genetically modified tobacco plants [Owen M et al. (1992) Biotechnology (NY) 10(7): 790-794; Franken E et al. (1997) Curr. Opin. Biotechnol. 8(4): 411-416; Whitelam (1996) Trend Plant Sci. 1: 286-272].

[0336.0.0.0] An "antisense" nucleic acid molecule comprises a nucleotide sequence, which is complementary to a "sense" nucleic acid molecule encoding a protein, e.g., complementary to the coding strand of a double-stranded cDNA molecule or

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complementary to an encoding mRNA sequence. Accordingly, an antisense nucleic acid molecule can bond via hydrogen bonds to a sense nucleic acid molecule. The antisense nucleic acid molecule can be complementary to an entire coding strand of a nucleic acid molecule conferring the expression of the polypeptide of the invention or used in the process of the present invention, as the nucleic acid molecule of the invention coding strand, or to only a portion thereof. Accordingly, an antisense nucleic acid molecule can be antisense to a "coding region" of the coding strand of a nucleotide sequence of a nucleic acid molecule of the present invention. The term "coding region" refers to the region of the nucleotide sequence comprising codons, which are translated into amino acid residues. Further, the antisense nucleic acid molecule is antisense to a "noncoding region" of the coding strand of a nucleotide sequence encoding the polypeptide of the invention or a polypeptide used in the process of the invention. The term "noncoding region" refers to 5' and 3' sequences which flank the coding region that are not translated into a polypeptide, i.e., also referred to as 5' and 3' untranslated regions (5'-UTR or 3'-UTR).

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[0337.0.0.0] Given the coding strand sequences encoding the polypeptide of the present invention antisense nucleic acid molecules of the invention can be designed according to the rules of Watson and Crick base pairing.

[0338.0.0.0] The antisense nucleic acid molecule can be complementary to the entire 20 coding region of the mRNA encoding the nucleic acid molecule ot the invention or used in the process of the present invention, but can also be an oligonucleotide which is antisense to only a portion of the coding or noncoding region of said mRNA. For example, the antisense oligonucleotide can be complementary to the region surrounding the translation start site of said mRNA. An antisense oligonucleotide can 25 be, for example, about 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 100 or 200 nucleotides in length. An antisense nucleic acid molecule of the invention can be constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, an antisense nucleic acid molecule (e.g., an antisense oligonucleotide) can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to 30 increase the physical stability of the duplex formed between the antisense and sense nucleic acids, e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used. Examples of modified nucleotides which can be used to generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, 35 hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil. dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-40 methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-Dmannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3)w, and 2,6-diaminopurine. Alternatively, the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid molecule has been subcloned in an antisense orientation (i.e., RNA transcribed from the inserted nucleic acid molecule will be of an antisense orientation to a target nucleic acid molecule of interest, described further in the following subsection).

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- 10 [0339.0.0.0] The antisense nucleic acid molecules of the invention are typically administered to a cell or generated *in situ* such that they hybridize with or bind to cellular mRNA and/or genomic DNA encoding a polypeptide of the invention having aforementioned the fine chemical increasing activity to thereby inhibit expression of the protein, e.g., by inhibiting transcription and/or translation.
- [0340.0.0.0] The hybridization can be by conventional nucleotide complementarity to form a stable duplex, or, for example, in the case of an antisense nucleic acid molecule which binds to DNA duplexes, through specific interactions in the major groove of the double helix. The antisense nucleic acid molecule can also be delivered to cells using the vectors described herein. To achieve sufficient intracellular concentrations of the antisense molecules, vector in which the antisense nucleic acid molecule is placed under the control of a strong prokaryotic, viral, or eukaryotic including plant promoters are preferred.
  - [0341.0.0.0] In a further embodiment, the antisense nucleic acid molecule of the invention can be an α-anomeric nucleic acid molecule. A α-anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual units, the strands run parallel to each other (Gaultier et al. (1987) *Nucleic Acids. Res.* 15:6625-6641). The antisense nucleic acid molecule can also comprise a 2'-o-methylribonucleotide (Inoue et al. (1987) *Nucleic Acids Res.* 15:6131-6148) or a chimeric RNA-DNA analogue (Inoue et al. (1987) *FEBS Lett.* 215:327-330).
- [0342.0.0.0] Further the antisense nucleic acid molecule of the invention can be also a ribozyme. Ribozymes are catalytic RNA molecules with ribonuclease activity, which are capable of cleaving a single-stranded nucleic acid, such as an mRNA, to which they have a complementary region. Thus, ribozymes (e.g., hammerhead ribozymes (described in Haselhoff and Gerlach (1988) Nature 334:585-591)) can be used to catalytically cleave mRNA transcripts encoding the polypeptide of the invention to thereby inhibit translation of said mRNA. A ribozyme having specificity for a nucleic acid molecule encoding the polypeptide of the invention or used in the process of the invention can be designed based upon the nucleotide sequence of the invention or on

the basis of a heterologous sequence to be isolated according to methods taught in this invention. For example, a derivative of a *Tetrahymena* L-19 IVS RNA can be constructed in which the nucleotide sequence of the active site is complementary to the nucleotide sequence to be cleaved in an encoding mRNA. See, e.g., Cech et al. U.S. Patent No. 4,987,071 and Cech et al. U.S. Patent No. 5,116,742. Alternatively, mRNA encoding the polypeptide of the invention or a polypeptide used in the process of the invention can be used to select a catalytic RNA having a specific ribonuclease activity from a pool of RNA molecules. See, e.g., Bartel, D. and Szostak, J.W. (1993) *Science* 261:1411-1418.

- [0343.0.0.0] The antisense molecule of the present invention comprises also a nucleic acid molecule comprising a nucleotide sequences complementary to the regulatory region of an nucleotide sequence encoding the natural occurring polypeptide of the invention, e.g. the polypeptide sequences shown in the sequence listing, or identified according to the methods described herein, e.g., its promoter and/or enhancers, e.g. to form triple helical structures that prevent transcription of the gene in target cells. See generally, Helene, C. (1991) Anticancer Drug Des. 6(6): 569-84; Helene, C. et al. (1992) Ann. N.Y. Acad. Sci. 660:27-36; and Maher, L.J. (1992) Bioassays 14(12):807-15.
  - [0344.0.0.0] Furthermore the present invention relates to a double stranded RNA molecule capable for the reduction or inhibition of the activity of the gene product of a gene encoding the polypeptide of the invention, a polypeptide used in the process of the invention, the nucleic acid molecule of the invention or a nucleic acid molecule used in the process of the invention encoding.

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The method of regulating genes by means of double-stranded RNA ("double-stranded RNA interference"; dsRNAi) has been described extensively for animal, yeast, fungi and plant organisms such as Neurospora, zebrafish, Drosophila, mice, planaria, humans, Trypanosoma, petunia or Arabidopsis (for example Matzke MA et al. (2000) Plant Mol. Biol. 43: 401-415; Fire A. et al. (1998) Nature 391: 806-811; WO 99/32619; WO 99/53050; WO 00/68374; WO 00/44914; WO 00/44895; WO 00/49035; WO 00/63364). In addition RNAi is also documented as an advantageously tool for the repression of genes in bacteria such as E. coli for example by Tchurikov et al. [J. Biol. Chem., 2000, 275 (34): 26523 - 26529]. Fire et al. named the phenomenon RNAi for "RNA interference". The techniques and methods described in the above references are expressly referred to. Efficient gene suppression can also be observed in the case of transient expression or following transient transformation, for example as the consequence of a biolistic transformation (Schweizer P et al. (2000) Plant J 2000 24: 895-903); dsRNAi methods are based on the phenomenon that the simultaneous introduction of complementary strand and counterstrand of a gene transcript brings about highly effective suppression of the expression of the gene in question. The

resulting phenotype is very similar to that of an analogous knock-out mutant (Waterhouse PM et al. (1998) Proc. Natl. Acad. Sci. USA 95: 13959-64).

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Tuschl et al. [Gens Dev., 1999, 13 (24): 3191 - 3197] was able to [0346.0.0.0] show that the efficiency of the RNAi method is a function of the length of the duplex, the length of the 3'-end overhangs, and the sequence in these overhangs. Based on the work of Tuschl et al. the following guidelines can be given to the skilled worker: To achieve good results the 5' and 3' untranslated regions of the used nucleic acid sequence and regions close to the start codon should be avoided as this regions are richer in regulatory protein binding sites and interactions between RNAi sequences and such regulatory proteins might lead to undesired interactions. Preferably a region of the 10 used mRNA is selected, which is 50 to 100 nt (= nucleotides or bases) downstream of the AUG start codon. Only dsRNA (= double-stranded RNA) sequences from exons are useful for the method, as sequences from introns have no effect. The G/C content in this region should be greater than 30% and less than 70% ideally around 50%. A possible secondary structure of the target mRNA is less important for the effect of the 15 RNAi method.

[0347.0.0.0] The dsRNAi method has proved to be particularly effective and advantageous for reducing the expression of the nucleic acid sequences of the SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 20 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 25 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 and/or homologs thereof. As described inter alia in WO 99/32619, dsRNAi approaches are clearly superior to 30 traditional antisense approaches. The invention therefore furthermore relates to double-stranded RNA molecules (dsRNA molecules) which, when introduced into an organism, advantageously into a plant (or a cell, tissue, organ or seed derived therefrom), bring about altered metabolic activity by the reduction in the expression of the nucleic acid sequences of the SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 35 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 40 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253,

255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 and/or homologs thereof. In a double-stranded RNA molecule for reducing the expression of an protein encoded by a nucleic acid sequence of one of the SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 10 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 15 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 and/or homologs thereof, one of the two RNA strands is essentially identical to at least part of a nucleic acid sequence, and the respective other RNA strand is essentially identical to at least part 20 of the complementary strand of a nucleic acid sequence.

[0348.0.0.0] The term "essentially identical" refers to the fact that the dsRNA sequence may also include insertions, deletions and individual point mutations in comparison to the target sequence while still bringing about an effective reduction in expression. Preferably, the homology as defined above amounts to at least 30%, 25 preferably at least 40%, 50%, 60%, 70% or 80%, very especially preferably at least 90%, most preferably 100%, between the "sense" strand of an inhibitory dsRNA and a part-segment of a nucleic acid sequence of the invention (or between the "antisense" strand and the complementary strand of a nucleic acid sequence, respectively). The part-segment amounts to at least 10 bases, preferably at least 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 bases, especially preferably at least 40, 50, 60, 70, 80 30 or 90 bases, very especially preferably at least 100, 200, 300 or 400 bases, most preferably at least 500, 600, 700, 800, 900 or more bases or at least 1000 or 2000 bases or more in length. In another preferred embodiment of the invention the partsegment amounts to 17, 18, 19, 20, 21, 22, 23, 24, 25, 26 or 27 bases, preferably to 35 20, 21, 22, 23, 24 or 25 bases. These short sequences are preferred in animals and plants. The longer sequences preferably between 200 and 800 bases are preferred in nonmammalian animals, preferably in invertebrates, in yeast, fungi or bacteria, but they are also useable in plants. Long double-stranded RNAs are processed in the organisms into many siRNAs (= small/short interfering RNAs) for example by the 40 protein Dicer, which is a ds-specific Rnase III enzyme. As an alternative, an "essentially identical" dsRNA may also be defined as a nucleic acid sequence, which is capable of

hybridizing with part of a gene transcript (for example in 400 mM NaCl, 40 mM PIPES pH 6.4, 1 mM EDTA at 50°C or 70°C for 12 to 16 h).

[0349.0.0.0] The dsRNA may consist of one or more strands of polymerized ribonucleotides. Modification of both the sugar-phosphate backbone and of the nucleosides may furthermore be present. For example, the phosphodiester bonds of the natural RNA can be modified in such a way that they encompass at least one nitrogen or sulfur heteroatom. Bases may undergo modification in such a way that the activity of, for example, adenosine deaminase is restricted. These and other modifications are described herein below in the methods for stabilizing antisense RNA.

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10 [0350.0.0.0] The dsRNA can be prepared enzymatically; it may also be synthesized chemically, either in full or in part.

[0351.0.0.0] The double-stranded structure can be formed starting from a single, self-complementary strand or starting from two complementary strands. In a single, self-complementary strand, "sense" and "antisense" sequence can be linked by a linking sequence ("linker") and form for example a hairpin structure. Preferably, the linking sequence may take the form of an intron, which is spliced out following dsRNA synthesis. The nucleic acid sequence encoding a dsRNA may contain further elements such as, for example, transcription termination signals or polyadenylation signals. If the two strands of the dsRNA are to be combined in a cell or an organism advantageously in a plant, this can be brought about in a variety of ways.

**[0352.0.0.0]** Formation of the RNA duplex can be initiated either outside the cell or within the cell. As shown in WO 99/53050, the dsRNA may also encompass a hairpin structure, by linking the "sense" and "antisense" strands by a "linker" (for example an intron). The self-complementary dsRNA structures are preferred since they merely require the expression of a construct and always encompass the complementary strands in an equimolar ratio.

[0353.0.0.0] The expression cassettes encoding the "antisense" or the "sense" strand of the dsRNA or the self-complementary strand of the dsRNA are preferably inserted into a vector and stably inserted into the genome of a plant, using the methods described herein below (for example using selection markers), in order to ensure permanent expression of the dsRNA.

[0354.0.0.0] The dsRNA can be introduced using an amount which makes possible at least one copy per cell. A larger amount (for example at least 5, 10, 100, 500 or 1 000 copies per cell) may bring about more efficient reduction.

[0355.0.0.0] As has already been described, 100 % sequence identity between the dsRNA and a gene transcript of a nucleic acid sequence of one of the SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57,

59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 or it's homolog is not necessarily 10 required in order to bring about effective reduction in the expression. The advantage is, accordingly, that the method is tolerant with regard to sequence deviations as may be present as a consequence of genetic mutations, polymorphisms or evolutionary divergences. Thus, for example, using the dsRNA, which has been generated starting from a sequence of one of SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 15 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 20 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 25 393 or homologs thereof of the one organism, may be used to suppress the corresponding expression in another organism.

[0356.0.0.0] Due to the high degree of sequence homology between sequences from various organisms (e. g. plants), allows the conclusion that these proteins may be conserved to a high degree within, for example other, plants, it is optionally possible that the expression of a dsRNA derived from one of the disclosed sequences as shown herein or homologs thereof should also have has an advantageous effect in other plant species. Preferably the consensus sequences shown herein can be used for the construction of useful dsRNA molecules.

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[0357.0.0.0] The dsRNA can be synthesized either in vivo or in vitro. To this end, a DNA sequence encoding a dsRNA can be introduced into an expression cassette under the control of at least one genetic control element (such as, for example, promoter, enhancer, silencer, splice donor or splice acceptor or polyadenylation signal). Suitable advantageous constructs are described herein below. Polyadenylation is not required, nor do elements for initiating translation have to be present.

[0358.0.0.0] A dsRNA can be synthesized chemically or enzymatically. Cellular RNA polymerases or bacteriophage RNA polymerases (such as, for example T3, T7 or SP6 RNA polymerase) can be used for this purpose. Suitable methods for the in-vitro expression of RNA are described (WO 97/32016; US 5,593,874; US 5,698,425, US 5,712,135, US 5,789,214, US 5,804,693). Prior to introduction into a cell, tissue or organism, a dsRNA which has been synthesized in vitro either chemically or enzymatically can be isolated to a higher or lesser degree from the reaction mixture, for example by extraction, precipitation, electrophoresis, chromatography or combinations of these methods. The dsRNA can be introduced directly into the cell or else be applied extracellularly (for example into the interstitial space).

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- [0359.0.0.0] Advantageously the RNAi method leads to only a partial loss of gene function and therefore enables the skilled worker to study a gene dose effect in the disered organism and to fine tune the process of the invention. Futhermore it enables a person skilled in the art to study multiple functions of a gene.
- 15 [0360.0.0.0] Stable transformation of the plant with an expression construct, which brings about the expression of the dsRNA is preferred, however. Suitable methods are described herein below.
  - [0361.0.0.0] A further embodiment of the invention also relates to a method for the generation of a transgenic host or host cell, e.g. a eukaryotic or prokaryotic cell, preferably a transgenic microorganism, a transgenic plant cell or a transgenic plant tissue or a transgenic plant, which comprises introducing, into the plant, the plant cell or the plant tissue, the nucleic acid construct according to the invention, the vector according to the invention, or the nucleic acid molecule according to the invention.
- [0362.0.0.0] A further embodiment of the invention also relates to a method for the transient generation of a host or host cell, eukaryotic or prokaryotic cell, preferably a transgenic microorganism, a transgenic plant cell or a transgenic plant tissue or a transgenic plant, which comprises introducing, into the plant, the plant cell or the plant tissue, the nucleic acid construct according to the invention, the vector according to the invention, the nucleic acid molecule characterized herein as being contained in the nucleic acid construct of the invention or the nucleic acid molecule according to the invention, whereby the introduced nucleic acid molecules, nucleic acid construct and/or vector is not integrated into the genome of the host or host cell. Therefore the transformants are not stable during the propagation of the host in respect of the introduced nucleic acid molecules, nucleic acid construct and/or vector.
- [0363.0.0.0] In the process according to the invention, transgenic organisms are also to be understood as meaning if they take the form of plants plant cells, plant tissues, plant organs such as root, shoot, stem, seed, flower, tuber or leaf, or intact plants which are grown for the production of the fine chemical.

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[0364.0.0.0] Growing is to be understood as meaning for example culturing the transgenic plant cells, plant tissue or plant organs on or in a nutrient medium or the intact plant on or in a substrate, for example in hydroponic culture, potting compost or on a field soil.

- [0365.0.0.0] In a further advantageous embodiment of the process, the nucleic acid molecules can be expressed in single-celled plant cells (such as algae), see Falciatore et al., 1999, Marine Biotechnology 1 (3): 239-251 and references cited therein, and plant cells from higher plants (for example spermatophytes such as crops). Examples of plant expression vectors encompass those which are described in detail herein or in:
  Becker, D. [(1992) Plant Mol. Biol. 20:1195-1197] and Bevan, M.W. [(1984), Nucl. Acids Res. 12:8711-8721; Vectors for Gene Transfer in Higher Plants; in: Transgenic Plants, Vol. 1, Engineering and Utilization, Ed.: Kung and R. Wu, Academic Press, 1993, pp. 15-38]. An overview of binary vectors and their use is also found in Hellens, R. [(2000), Trends in Plant Science, Vol. 5 No.10, 446-451.
- [0366.0.0.0] Vector DNA can be introduced into prokaryotic or eukaryotic cells via 15 conventional transformation or transfection techniques. The terms "transformation" and "transfection" include conjugation and transduction and, as used in the present context, are intended to encompass a multiplicity of prior-art methods for introducing foreign nucleic acid molecules (for example DNA) into a host cell, including calcium phosphate coprecipitation or calcium chloride coprecipitation, DEAE-dextran-mediated 20 transfection, PEG-mediated transfection, lipofection, natural competence, chemically mediated transfer, electroporation or particle bombardment. Suitable methods for the transformation or transfection of host cells, including plant cells, can be found in Sambrook et al. (Molecular Cloning: A Laboratory Manual., 2nd Ed., Cold Spring 25 Harbor Laboratory, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989) and in other laboratory handbooks such as Methods in Molecular Biology, 1995, Vol. 44, Agrobacterium protocols, Ed.: Gartland and Davey, Humana Press, Totowa, New Jersey.
  - [0367.0.0.0] The above-described methods for the transformation and regeneration of plants from plant tissues or plant cells are exploited for transient or stable transformation of plants. Suitable methods are the transformation of protoplasts by polyethylene-glycol-induced DNA uptake, the biolistic method with the gene gun known as the particle bombardment method -, electroporation, the incubation of dry embryos in DNA-containing solution, microinjection and the Agrobacterium-mediated gene transfer. The abovementioned methods are described for example in B. Jenes, Techniques for Gene Transfer, in: Transgenic Plants, Vol. 1, Engineering and Utilization, edited by S.D. Kung and R. Wu, Academic Press (1993) 128-143 and in Potrykus Annu. Rev. Plant Physiol. Plant Molec. Biol. 42 (1991) 205-225. The construct to be expressed is preferably cloned into a vector, which is suitable for transforming Agrobacterium tumefaciens, for example pBin19 (Bevan, Nucl. Acids Res. 12 (1984)

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8711). Agrobacteria transformed with such a vector can then be used in the known manner for the transformation of plants, in particular crop plants, such as, for example, tobacco plants, for example by bathing scarified leaves or leaf segments in an agrobacterial solution and subsequently culturing them in suitable media. The transformation of plants with Agrobacterium tumefaciens is described for example by Höfgen and Willmitzer in Nucl. Acid Res. (1988) 16, 9877 or known from, inter alia, F.F. White, Vectors for Gene Transfer in Higher Plants; in Transgenic Plants, Vol. 1, Engineering and Utilization, edited by S.D. Kung and R. Wu, Academic Press, 1993, pp. 15-38.

[0368.0.0.0] To select for the successful transfer of the nucleic acid molecule, vector 10 or nucleic acid construct of the invention according to the invention into a host organism, it is advantageous to use marker genes as have already been described above in detail. It is known of the stable or transient integration of nucleic acids into plant cells that only a minority of the cells takes up the foreign DNA and, if desired, integrates it into its genome, depending on the expression vector used and the 15 transfection technique used. To identify and select these integrants, a gene encoding for a selectable marker (as described above, for example resistance to antibiotics) is usually introduced into the host cells together with the gene of interest. Preferred selectable markers in plants comprise those, which confer resistance to an herbicide such as glyphosate or gluphosinate. Other suitable markers are, for example, markers, 20 which encode genes involved in biosynthetic pathways of, for example, sugars or amino acids, such as ß-galactosidase, ura3 or ilv2. Markers, which encode genes such as luciferase, gfp or other fluorescence genes, are likewise suitable. These markers and the aforementioned markers can be used in mutants in whom these genes are not functional since, for example, they have been deleted by conventional methods. 25 Furthermore, nucleic acid molecules, which encode a selectable marker, can be introduced into a host cell on the same vector as those, which encode the polypeptides of the invention or used in the process or else in a separate vector. Cells which have been transfected stably with the nucleic acid introduced can be identified for example by selection (for example, cells which have integrated the selectable marker survive 30 whereas the other cells die).

[0369.0.0.0] Since the marker genes, as a rule specifically the gene for resistance to antibiotics and herbicides, are no longer required or are undesired in the transgenic host cell once the nucleic acids have been introduced successfully, the process according to the invention for introducing the nucleic acids advantageously employs techniques which enable the removal, or excision, of these marker genes. One such a method is what is known as cotransformation. The cotransformation method employs two vectors simultaneously for the transformation, one vector bearing the nucleic acid according to the invention and a second bearing the marker gene(s). A large proportion of transformants receives or, in the case of plants, comprises (up to 40% of the transformants and above), both vectors. In case of transformation with Agrobacteria,

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the transformants usually receive only a part of the vector, the sequence flanked by the T-DNA which usually represents the expression cassette. The marker genes can subsequently be removed from the transformed plant by performing crosses. In another method, marker genes integrated into a transposon are used for the transformation together with desired nucleic acid (known as the Ac/Ds technology). The transformants can be crossed with a transposase resource or the transformants are transformed with a nucleic acid construct conferring expression of a transposase, transiently or stable. In some cases (approx. 10%), the transposon jumps out of the genome of the host cell once transformation has taken place successfully and is lost. In a further number of cases, the transposon jumps to a different location. In these cases, the marker gene must be eliminated by performing crosses. In microbiology, techniques were developed which make possible, or facilitate, the detection of such events. A further advantageous method relies on what are known as recombination systems, whose advantage is that elimination by crossing can be dispensed with. The best-known system of this type is what is known as the Cre/lox system. Cre1 is a recombinase, which removes the sequences located between the loxP sequences. If the marker gene is integrated between the loxP sequences, it is removed, once transformation has taken place successfully, by expression of the recombinase. Further recombination systems are the HIN/HIX, FLP/FRT and REP/STB system (Tribble et al., J. Biol. Chem., 275, 2000: 22255-22267; Velmurugan et al., J. Cell Biol., 149, 2000: 553-566). A site-specific integration into the plant genome of the nucleic acid sequences according to the invention is possible. Naturally, these methods can also be applied to microorganisms such as yeast, fungi or bacteria.

[0370.0.0.0] Agrobacteria transformed with an expression vector according to the invention may also be used in the manner known per se for the transformation of plants such as experimental plants like Arabidopsis or crop plants, such as, for example, cereals, maize, oats, rye, barley, wheat, soya, rice, cotton, sugarbeet, canola, sunflower, flax, hemp, potato, tobacco, tomato, carrot, bell peppers, oilseed rape, tapioca, cassava, arrow root, tagetes, alfalfa, lettuce and the various tree, nut, and grapevine species, in particular oil-containing crop plants such as soya, peanut, castoroil plant, sunflower, maize, cotton, flax, oilseed rape, coconut, oil palm, safflower (Carthamus tinctorius) or cocoa beans, for example by bathing scarified leaves or leaf segments in an agrobacterial solution and subsequently growing them in suitable media.

[0371.0.0.0] In addition to the transformation of somatic cells, which then has to be regenerated into intact plants, it is also possible to transform the cells of plant meristems and in particular those cells which develop into gametes. In this case, the transformed gametes follow the natural plant development, giving rise to transgenic plants. Thus, for example, seeds of Arabidopsis are treated with agrobacteria and seeds are obtained from the developing plants of which a certain proportion is transformed and thus transgenic (Feldman, KA and Marks MD (1987). Mol Gen Genet

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208:274-289; Feldmann K (1992). In: C Koncz, N-H Chua and J Shell, eds, Methods in Arabidopsis Research. Word Scientific, Singapore, pp. 274-289). Alternative methods are based on the repeated removal of the influorescences and incubation of the excision site in the center of the rosette with transformed agrobacteria, whereby transformed seeds can likewise be obtained at a later point in time (Chang (1994). 5 Plant J. 5: 551-558; Katavic (1994). Mol Gen Genet, 245: 363-370). However, an especially effective method is the vacuum infiltration method with its modifications such as the "floral dip" method. In the case of vacuum infiltration of Arabidopsis, intact plants under reduced pressure are treated with an agrobacterial suspension (Bechthold, N (1993). C R Acad Sci Paris Life Sci, 316: 1194-1199), while in the case of the "floral dip" 10 method the developing floral tissue is incubated briefly with a surfactant-treated agrobacterial suspension (Clough, SJ und Bent, AF (1998). The Plant J. 16, 735-743). A certain proportion of transgenic seeds are harvested in both cases, and these seeds can be distinguished from nontransgenic seeds by growing under the above-described selective conditions. In addition the stable transformation of plastids is of advantages 15 because plastids are inherited maternally is most crops reducing or eliminating the risk of transgene flow through pollen. The transformation of the chloroplast genome is generally achieved by a process, which has been schematically displayed in Klaus et al., 2004 (Nature Biotechnology 22(2), 225-229). Briefly the sequences to be transformed are cloned together with a selectable marker gene between flanking 20 sequences homologous to the chloroplast genome. These homologous flanking sequences direct site-specific integration into the plastome. Plastidal transformation has been described for many different plant species and an overview can be taken from Bock (2001) Transgenic plastids in basic research and plant biotechnology. J Mol Biol. 2001 Sep 21; 312(3): 425-38 or Maliga, P (2003) Progress towards 25 commercialization of plastid transformation technology. Trends Biotechnol. 21, 20-28. Further biotechnological progress has recently been reported in form of marker free plastid transformants, which can be produced by a transient cointegrated maker gene (Klaus et al., 2004, Nature Biotechnology 22(2), 225-229).

30 [0372.0.0.0] The genetically modified plant cells can be regenerated via all methods with which the skilled worker is familiar. Suitable methods can be found in the abovementioned publications of S.D. Kung and R. Wu, Potrykus or Höfgen and Willmitzer.

[0373.0.0.0] Accordingly, the present invention thus also relates to a plant cell comprising the nucleic acid construct according to the invention, the nucleic acid molecule according to the invention or the vector according to the invention.

[0374.0.0.0] Accordingly the present invention relates to any cell transgenic for any nucleic acid characterized as part of the invention, e.g. conferring the increase of the fine chemical in a cell or an organism or a part thereof, e.g. the nucleic acid molecule of the invention, the nucleic acid construct of the invention, the antisense molecule of the

invention, the vector of the invention or a nucleic acid molecule encoding the polypeptide of the invention, e.g. encoding a polypeptide having the biological activity of the protein of the invention. Due to the above mentioned activity the fine chemical content in a cell or an organism is increased. For example, due to modulation or manupulation, the cellular activity is increased, e.g. due to an increased expression or specific activity of the subject matters of the invention in a cell or an organism or a part thereof. Transgenic for a polypeptide having biological activity of the protein of the invention or activity means herein that due to modulation or manipulation of the genome, the biological activity of the protein of the invention is increased in the cell or organism or part thereof. Examples are described above in context with the process of the invention

[0375.0.0.0] "Transgenic", for example regarding a nucleic acid molecule, an nucleic acid construct or a vector comprising said nucleic acid molecule or an organism transformed with said nucleic acid molecule, nucleic acid construct or vector, refers to all those subjects originating by recombinant methods in which either

- a) the nucleic acid sequence, or
- b) a genetic control sequence linked operably to the nucleic acid sequence, for example a promoter, or
- c) (a) and (b)

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- are not located in their natural genetic environment or have been modified by recombinant methods, an example of a modification being a substitution, addition, deletion, inversion or insertion of one or more nucleotide residues. Natural genetic environment refers to the natural chromosomal locus in the organism of origin, or to the presence in a genomic library. In the case of a genomic library, the natural genetic environment of the nucleic acid sequence is preferably retained, at least in part. The environment flanks the nucleic acid sequence at least at one side and has a sequence of at least 50 bp, preferably at least 500 bp, especially preferably at least 1000 bp, very especially preferably at least 5000 bp, in length.
- [0376.0.0.0] A naturally occurring expression cassette for example the naturally occurring combination of the promoter of the protein of the invention with the corresponding protein gene becomes a transgenic expression cassette when it is modified by non-natural, synthetic "artificial" methods such as, for example, mutagenization. Such methods have been described (US 5,565,350; WO 00/15815; also see above).
- [0377.0.0.0] Further, the plant cell, plant tissue or plant can also be transformed such that further enzymes and proteins are (over)expressed which expression supports an increase of the fine chemical.

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[0378.0.0.0] However, transgenic also means that the nucleic acids according to the invention are located at their natural position in the genome of an organism, but that the sequence has been modified in comparison with the natural sequence and/or that the regulatory sequences of the natural sequences have been modified. Preferably, transgenic/recombinant is to be understood as meaning the transcription of the nucleic acids used in the process according to the invention occurs at a non-natural position in the genome, that is to say the expression of the nucleic acids is homologous or, preferably, heterologous. This expression can be transiently or of a sequence integrated stably into the genome.

[0379.0.0.0] The term "transgenic plants" used in accordance with the invention also 10 refers to the progeny of a transgenic plant, for example the T<sub>1</sub>, T<sub>2</sub>, T<sub>3</sub> and subsequent plant generations or the BC<sub>1</sub>, BC<sub>2</sub>, BC<sub>3</sub> and subsequent plant generations. Thus, the transgenic plants according to the invention can be raised and selfed or crossed with other individuals in order to obtain further transgenic plants according to the invention. Transgenic plants may also be obtained by propagating transgenic plant cells 15 vegetatively. The present invention also relates to transgenic plant material, which can be derived from a transgenic plant population according to the invention. Such material includes plant cells and certain tissues, organs and parts of plants in all their manifestations, such as seeds, leaves, anthers, fibers, tubers, roots, root hairs, stems, embryo, calli, cotelydons, petioles, harvested material, plant tissue, reproductive tissue 20 and cell cultures, which are derived from the actual transgenic plant and/or can be used for bringing about the transgenic plant.

[0380.0.0.0] Any transformed plant obtained according to the invention can be used in a conventional breeding scheme or in in vitro plant propagation to produce more transformed plants with the same characteristics and/or can be used to introduce the same characteristic in other varieties of the same or related species. Such plants are also part of the invention. Seeds obtained from the transformed plants genetically also contain the same characteristic and are part of the invention. As mentioned before, the present invention is in principle applicable to any plant and crop that can be transformed with any of the transformation method known to those skilled in the art. Another embodiment of the invention is the use of the nucleic acid molecule as claimed in above in mapping and breeding processes for the identification of plant varieties having and increased capacity for production of the fine chemical.

[0381.0.0.0] In an especially preferred embodiment, the organism, the host cell, plant cell, plant, microorganism or plant tissue according to the invention is transgenic.

[0382.0.0.0] Accordingly, the invention therefore relates to transgenic organisms transformed with at least one nucleic acid molecule, nucleic acid construct or vector according to the invention, and to cells, cell cultures, tissues, parts - such as, for example, in the case of plant organisms, plant tissue, for example leaves, roots and the

like - or propagation material derived from such organisms, or intact plants. The terms "recombinant (host)", and "transgenic (host)" are used interchangeably in this context. Naturally, these terms refer not only to the host organism or target cell in question, but also to the progeny, or potential progeny, of these organisms or cells. Since certain modifications may occur in subsequent generations owing to mutation or environmental effects, such progeny is not necessarily identical with the parental cell, but still comes within the scope of the term as used herein.

[0383.0.0.0] Suitable organisms for the process according to the invention or as hosts are all these eukaryotic or prokaryotic organisms, which are capable of synthesizing the fine chemcial. The organisms used as hosts are microorganisms, such as bacteria, fungi, yeasts or algae, non-human animals, or plants, such as dictotyledonous or monocotyledonous plants.

[0384.0.0.0] In principle all plants can be used as host organism, especially the plants mentioned above as source organism. Preferred transgenic plants are, for example, selected from the families Aceraceae, Anacardiaceae, Apiaceae, Asteraceae, Brassicaceae, Cactaceae, Cucurbitaceae, Euphorbiaceae, Fabaceae, Malvaceae, Nymphaeaceae, Papaveraceae, Rosaceae, Salicaceae, Solanaceae, Arecaceae, Bromeliaceae, Cyperaceae, Iridaceae, Liliaceae, Orchidaceae, Gentianaceae, Labiaceae, Magnoliaceae, Ranunculaceae, Carifolaceae, Rubiaceae, Scrophulariaceae, 20 Caryophyllaceae, Ericaceae, Polygonaceae, Violaceae, Juncaceae or Poaceae and preferably from a plant selected from the group of the families Apiaceae, Asteraceae, Brassicaceae, Cucurbitaceae, Fabaceae, Papaveraceae, Rosaceae, Solanaceae. Liliaceae or Poaceae. Preferred are crop plants such as plants advantageously selected from the group of the genus peanut, oilseed rape, canola, sunflower, 25 safflower, olive, sesame, hazelnut, almond, avocado, bay, pumpkin/squash, linseed. soya, pistachio, borage, maize, wheat, rye, oats, sorghum and millet, triticale, rice, barley, cassava, potato, sugarbeet, egg plant, alfalfa, and perennial grasses and forage plants, oil palm, vegetables (brassicas, root vegetables, tuber vegetables, pod vegetables, fruiting vegetables, onion vegetables, leafy vegetables and stem 30 vegetables), buckwheat, Jerusalem artichoke, broad bean, vetches, lentil, dwarf bean, lupin, clover and Lucerne for mentioning only some of them.

[0385.0.0.0] Preferred plant cells, plant organs, plant tissues or parts of plants originate from the under source organism mentioned plant families, preferably from the abovementioned plant genus, more preferred from abovementioned plants spezies.

[0386.0.0.0] Transgenic plants comprising the fine chemical synthesized in the process according to the invention can be marketed directly without isolation of the compounds synthesized. In the process according to the invention, plants are understood as meaning all plant parts, plant organs such as leaf, stalk, root, tubers or seeds or propagation material or harvested material or the intact plant. In this context,

the seed encompasses all parts of the seed such as the seed coats, epidermal cells, seed cells, endosperm or embryonic tissue. The fine chemical produced in the process according to the invention may, however, also be isolated from the plant in free or bound form. The fine chemical produced by this process can be harvested by harvesting the organisms either from the culture in which they grow or from the field. This can be done via expressing, grinding and/or extraction, salt precipitation and/or ion-exchange chromatography of the plant parts, preferably the plant seeds, plant fruits, plant tubers and the like.

[0387.0.0.0] In a further embodiment, the present invention relates to a process for the generation of a microorganism, comprising the introduction, into the microorganism or parts thereof, of the nucleic acid construct of the invention, or the vector of the invention or the nucleic acid molecule of the invention.

[0388.0.0.0] In another embodiment, the present invention relates also to a transgenic microorganism comprising the nucleic acid molecule of the invention, the nucleic acid construct of the invention or the vector as of the invention. Appropriate microorganisms have been described herein before under source organism, preferred are in particular aforementioned strains suitable for the production of fine chemicals.

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[0389.0.0.0] Accordingly, the present invention relates also to a process according to the present invention whereby the produced fine chemical or fine chemical composition is isolated.

[0390.0.0.0] In this manner, more than 50% by weight, advantageously more than 60% by weight, preferably more than 70% by weight, especially preferably more than 80% by weight, very especially preferably more than 90% by weight, of the fine chemical produced in the process can be isolated. The resulting fine chemical can, if appropriate, subsequently be further purified, if desired mixed with other active ingredients such as vitamins, amino acids, carbohydrates, antibiotics and the like, and, if appropriate, formulated.

[0391.0.0.0] The fine chemical obtained in the process is suitable as starting material for the synthesis of further products of value. For example, they can be used in combination with other ingredients or alone for the production of pharmaceuticals, foodstuffs, animal feeds or cosmetics. Accordingly, the present invention relates a method for the production of a pharmaceuticals, food stuff, animal feeds, nutrients or cosmetics comprising the steps of the process according to the invention, including the isolation of the fine chemical or fine chemical composition produced and if desired formulating the product with a pharmaceutical acceptable carrier or formulating the product in a form acceptable for an application in agriculture. A further embodiment according to the invention is the use of the fine chemical produced in the process or of

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the transgenic organisms in animal feeds, foodstuffs, medicines, food supplements, cosmetics or pharmaceuticals.

[0392.0.0.0] In principle all microorganisms can be used as host organism especially the ones mentioned under source organism above. It is advantageous to use in the process of the invention transgenic microorganisms such as fungi such as the genus Claviceps or Aspergillus or Gram-positive bacteria such as the genera Bacillus, Corynebacterium, Micrococcus, Brevibacterium, Rhodococcus, Nocardia, Caseobacter or Arthrobacter or Gram-negative bacteria such as the genera Escherichia, Flavobacterium or Salmonella or yeasts such as the genera Rhodotorula, Saccharomyces, Hansenula or Candida. Particularly advantageous organisms are 10 selected from the group of genera Corynebacterium, Brevibacterium, Escherichia, Bacillus, Rhodotorula, Saccharomyces, Hansenula, Candida, Claviceps or Flavobacterium. It is very particularly advantageous to use in the process of the invention microorganisms selected from the group of genera and species consisting of 15 Saccharomyces cerevisiae, Hansenula anomala, Candida utilis, Claviceps purpurea, Bacillus circulans, Bacillus subtilis, Bacillus sp., Brevibacterium albidum, Brevibacterium album, Brevibacterium cerinum, Brevibacterium flavum, Brevibacterium glutamigenes, Brevibacterium iodinum, Brevibacterium ketoglutamicum, Brevibacterium lactofermentum, Brevibacterium linens, Brevibacterium roseum, 20 Brevibacterium saccharolyticum, Brevibacterium sp., Corynebacterium acetoacidophilum, Corynebacterium acetoglutamicum, Corynebacterium ammoniagenes, Corynebacterium glutamicum (= Micrococcus glutamicum), Corynebacterium melassecola, Corynebacterium sp. or Escherichia coli, specifically Saccharomyces cerevisiae, Escherichia coli K12 and its described strains.

25 The process of the invention is, when the host organisms are microorganisms, advantageously carried out at a temperature between 0°C and 95°C. preferably between 10°C and 85°C, particularly preferably between 15°C and 75°C, very particularly preferably between 15°C and 45°C. The pH is advantageously kept at between pH 4 and 12, preferably between pH 6 and 9, particularly preferably between 30 pH 7 and 8, during this. The process of the invention can be operated batchwise, semibatchwise or continuously. A summary of known cultivation methods is to be found in the textbook by Chmiel (Bioprozeßtechnik 1. Einführung in die Bioverfahrenstechnik (Gustav Fischer Verlag, Stuttgart, 1991)) or in the textbook by Storhas (Bioreaktoren und periphere Einrichtungen (Vieweg Verlag, Braunschweig/Wiesbaden, 1994)). The 35 culture medium to be used must meet the requirements of the respective strains in a suitable manner. Descriptions of culture media for various microorganisms are present in the handbook "Manual of Methods for General Bacteriology" of the American Society for Bacteriology (Washington D. C., USA, 1981). These media, which can be employed according to the invention include, as described above, usually one or more carbon 40 sources, nitrogen sources, inorganic salts, vitamins and/or trace elements. Preferred carbon sources are sugars such as mono-, di- or polysaccharides. Examples of very

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good carbon sources are glucose, fructose, mannose, galactose, ribose, sorbose, ribulose, lactose, maltose, sucrose, raffinose, starch or cellulose. Sugars can also be added to the media via complex compounds such as molasses, or other byproducts of sugar refining. It may also be advantageous to add mixtures of various carbon sources. Other possible carbon sources are oils and fats such as, for example, soybean oil, sunflower oil, peanut oil and/or coconut fat, fatty acids such as, for example, palmitic acid, stearic acid and/or linoleic acid, alcohols and/or polyalcohols such as, for example, glycerol, methanol and/or ethanol and/or organic acids such as, for example, acetic acid and/or lactic acid. Nitrogen sources are usually organic or inorganic nitrogen compounds or materials, which contain these compounds. Examples of nitrogen sources include ammonia in liquid or gaseous form or ammonium salts such as ammonium sulfate, ammonium chloride, ammonium phosphate, ammonium carbonate or ammonium nitrate, nitrates, urea, amino acids or complex nitrogen sources such as corn steep liquor, soybean meal, soybean protein, yeast extract, meat extract and others. The nitrogen sources may be used singly or as a mixture. Inorganic 15 salt compounds, which may be present in the media include the chloride, phosphorus or sulfate salts of calcium, magnesium, sodium, cobalt, molybdenum, potassium, manganese, zinc, copper and iron.

[0394.0.0.0] For preparing sulfur-containing fine chemicals, in particular the fine chemical, it is possible to use as sulfur source inorganic sulfur-containing compounds such as, for example, sulfates, sulfites, dithionites, tetrathionates, thiosulfates, sulfides or else organic sulfur compounds such as mercaptans and thiols.

[0395.0.0.0] It is possible to use as phosphorus source phosphoric acid, potassium dihydrogenphosphate or dipotassium hydrogenphosphate or the corresponding sodium-containing salts. Chelating agents can be added to the medium in order to keep the metal ions in solution. Particularly suitable chelating agents include dihydroxyphenols such as catechol or protocatechuate, or organic acids such as citric acid. The fermentation media employed according to the invention for cultivating microorganisms normally also contain other growth factors such as vitamins or growth promoters, which include, for example, biotin, riboflavin, thiamine, folic acid, nicotinic acid, pantothenate and pyridoxine. Growth factors and salts are often derived from complex media components such as yeast extract, molasses, corn steep liquor and the like. Suitable precursors can moreover be added to the culture medium. The exact composition of the media compounds depends greatly on the particular experiment and is chosen individually for each specific case. Information about media optimization is obtainable from the textbook "Applied Microbiol. Physiology, A Practical Approach" (editors P.M. Rhodes, P.F. Stanbury, IRL Press (1997) pp. 53-73, ISBN 0 19 963577 3). Growth media can also be purchased from commercial suppliers such as Standard 1 (Merck) or BHI (Brain heart infusion, DIFCO) and the like. All media components are sterilized either by heat (1.5 bar and 121°C for 20 min) or by sterilizing filtration. The components can be sterilized either together or, if necessary, separately. All media

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components can be present at the start of the cultivation or optionally be added continuously or batchwise. The temperature of the culture is normally between 15°C and 45°C, preferably at 25°C to 40°C, and can be kept constant or changed during the experiment. The pH of the medium should be in the range from 5 to 8.5, preferably around 7. The pH for the cultivation can be controlled during the cultivation by adding basic compounds such as sodium hydroxide, potassium hydroxide, ammonia or aqueous ammonia or acidic compounds such as phosphoric acid or sulfuric acid. Foaming can be controlled by employing antifoams such as, for example fatty acid polyglycol esters. The stability of plasmids can be maintained by adding to the medium suitable substances having a selective effect, for example antibiotics. Aerobic conditions are maintained by introducing oxygen or oxygen-containing gas mixtures such as, for example ambient air into the culture. The temperature of the culture is normally from 20°C to 45°C and preferably from 25°C to 40°C. The culture is continued until formation of the desired product is at a maximum. This aim is normally achieved within 10 hours to 160 hours.

[0396.0.0.0] The fermentation broths obtained in this way, containing the fine chemical in particular for example amino acids such as L-methionine, L-threonine and/or L-lysine, normally have a dry matter content of from 7.5 to 25% by weight. Sugar-limited fermentation is additionally advantageous, at least at the end, but especially over at least 30% of the fermentation time. This means that the concentration of utilizable sugar in the fermentation medium is kept at, or reduced to, ≥ 0 to 3 g/l during this time. The fermentation broth is then processed further. Depending on requirements, the biomass can be removed entirely or partly by separation methods, such as, for example, centrifugation, filtration, decantation or a combination of these methods, from the fermentation broth or left completely in it. The fermentation broth can then be thickened or concentrated by known methods, such as, for example, with the aid of a rotary evaporator, thin-film evaporator, falling film evaporator, by reverse osmosis or by nanofiltration. This concentrated fermentation broth can then be worked up by freeze-drying, spray drying, spray granulation or by other processes.

[0397.0.0.0] However, it is also possible to purify the fine chemical produced further. For this purpose, the product-containing composition is subjected to a chromatography on a suitable resin, in which case the desired product or the impurities are retained wholly or partly on the chromatography resin. These chromatography steps can be repeated if necessary, using the same or different chromatography resins. The skilled worker is familiar with the choice of suitable chromatography resins and their most effective use. The purified product can be concentrated by filtration or ultrafiltration and stored at a temperature at which the stability of the product is a maximum.

[0398.0.0.0] The identity and purity of the isolated compound(s) can be determined by prior art techniques. These include high performance liquid chromatography (HPLC), spectroscopic methods, mass spectrometry (MS), staining methods, thin-layer

chromatography, NIRS, enzyme assay or microbiological assays. These analytical methods are summarized in: Patek et al. (1994) Appl. Environ. Microbiol. 60:133-140; Malakhova et al. (1996) Biotekhnologiya 11 27-32; and Schmidt et al. (1998) Bioprocess Engineer. 19:67-70. Ulmann's Encyclopedia of Industrial Chemistry (1996) Vol. A27, VCH: Weinheim, pp. 89-90, pp. 521-540, pp. 540-547, pp. 559-566, 575-581 and pp. 581-587; Michal, G (1999) Biochemical Pathways: An Atlas of Biochemistry and Molecular Biology, John Wiley and Sons; Fallon, A. et al. (1987) Applications of

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10 [0399.0.0.0] In yet another aspect, the invention also relates to harvestable parts and to propagation material of the transgenic plants according to the invention which either contain transgenic plant cells expressing a nucleic acid molecule according to the invention or which contains cells which show an increased cellular activity of the polypeptide of the invention, e.g. an increased expression level or higher activity of the described protein.

HPLC in Biochemistry in: Laboratory Techniques in Biochemistry and Molecular

- [0400.0.0.0] Harvestable parts can be in principle any useful parts of a plant, for example, flowers, pollen, seedlings, tubers, leaves, stems, fruit, seeds, roots etc. Propagation material includes, for example, seeds, fruits, cuttings, seedlings, tubers, rootstocks etc. Preferred are seeds, fruits, seedlings or tubers as harvestable or propagation material.
- [0401.0.0.0] The invention furthermore relates to the use of the transgenic organisms according to the invention and of the cells, cell cultures, parts such as, for example, roots, leaves and the like as mentioned above in the case of transgenic plant organisms derived from them, and to transgenic propagation material such as seeds or fruits and the like as mentioned above, for the production of foodstuffs or feeding stuffs, pharmaceuticals or fine chemicals.
- **[0402.0.0.0]** Accordingly in another embodiment, the present invention relates to the use of the nucleic acid molecule, the organism, e.g. the microorganism, the plant, plant cell or plant tissue, the vector, or the polypeptide of the present invention for making fine chemicals such as fatty acids, carotenoids, isoprenoids, vitamins, lipids, wax esters, (poly)saccharides and/or polyhydroxyalkanoates, and/or its metabolism products, in particular, steroid hormones, cholesterol, prostaglandin, triacylglycerols, bile acids and/or ketone bodies producing cells, tissues and/or plants. There are a number of mechanisms by which the yield, production, and/or efficiency of production of fatty acids, carotenoids, isoprenoids, vitamins, wax esters, lipids, (poly)saccharides and/or polyhydroxyalkanoates, and/or its metabolism products, in particular, steroid hormones, cholesterol, triacylglycerols, prostaglandin, bile acids and/or ketone bodies or further of above defined fine chemicals incorporating such an altered protein can be affected. In the case of plants, by e.g. increasing the expression of acetyl-CoA which is

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the basis for many products, e.g., fatty acids, carotenoids, isoprenoids, vitamines, lipids, (poly)saccharides, wax esters, and/or polyhydroxyalkanoates, and/or its metabolism products, in particular, prostaglandin, steroid hormones, cholesterol, triacylglycerols, bile acids and/or ketone bodies in a cell, it may be possible to increase the amount of the produced said compounds thus permitting greater ease of harvesting and purification or in case of plants more efficient partitioning. Further, one or more of said metabolism products, increased amounts of the cofactors, precursor molecules, and intermediate compounds for the appropriate biosynthetic pathways maybe required. Therefore, by increasing the number and/or activity of transporter proteins involved in the import of nutrients, such as carbon sources (i.e., sugars), nitrogen sources (i.e., amino acids, ammonium salts), phosphate, and sulfur, it may be possible to improve the production of acetyl CoA and its metabolism products as mentioned above, due to the removal of any nutrient supply limitations on the biosynthetic process. In particular, it may be possible to increase the yield, production, and/or efficiency of production of said compounds, e.g. fatty acids, carotenoids, isoprenoids, vitamins, was esters, lipids, (poly)saccharides, and/or polyhydroxyalkanoates, and/or its metabolism products, in particular, steroid hormones, cholesterol, prostaglandin, triacylglycerols, bile acids and/or ketone bodies molecules etc. in plants.

[0403.0.0.0] Furthermore preferred is a method for the recombinant production of pharmaceuticals or fine chemicals in host organisms, wherein a host organism is transformed with one of the above-described nucleic acid constructs comprising one or more structural genes which encode the desired fine chemical or catalyze the biosynthesis of the desired fine chemical, the transformed host organism is cultured. and the desired fine chemical is isolated from the culture medium. This method can be applied widely to fine chemicals such as enzymes, vitamins, amino acids, sugars, fatty acids, and natural and synthetic flavorings, aroma substances and colorants or compositions comprising these. Especially preferred is the additional production of further amino acids, tocopherols and tocotrienols and carotenoids or compositions comprising said compounds. The transformed host organisms are cultured and the products are recovered from the host organisms or the culture medium by methods known to the skilled worker or the organism itself servers as food or feed supplement. The production of pharmaceuticals such as, for example, antibodies or vaccines, is described by Hood EE, Jilka JM. Curr Opin Biotechnol. 1999 Aug; 10(4): 382-6; Ma JK, Vine ND. Curr Top Microbiol Immunol. 1999; 236:275-92.

35 [0404.0.0.0] In one embodiment, the present invention relates to a method for the identification of a gene product conferring an increase in the fine chemical production in a cell, comprising the following steps:

(a) contacting, e.g. hybridising, the nucleic acid molecules of a sample, e.g. cells, tissues, plants or microorganisms or a nucleic acid library, which can contain a candidate gene encoding a gene product conferring an increase in the fine

chemical after expression, with the nucleic acid molecule of the present invention;

- identifying the nucleic acid molecules, which hybridize under relaxed stringent (b) conditions with the nucleic acid molecule of the present invention in particular to the nucleic acid molecule sequence shown in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 5 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169. 171. 173. 175. 177. 179. 181, 183, 185, 187, 189, 191, 193, 195, 197, 199<u>.</u> 10 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 15 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 and, optionally, isolating the full length cDNA clone or complete genomic clone;
- (c) introducing the candidate nucleic acid molecules in host cells, preferably in a plant cell or a microorganism, appropriate for producing the fine chemical;
  - (d) expressing the identified nucleic acid molecules in the host cells;
  - (e) assaying the the fine chemical level in the host cells; and
- identifying the nucleic acid molecule and its gene product which expression confers an increase in the the fine chemical level in the host cell after expression compared to the wild type.
- [0405.0.0.0] Relaxed hybridisation conditions are: After standard hybridisation procedures washing steps can be performed at low to medium stringency conditions usually with washing conditions of 40°-55°C and salt conditions between 2xSSC and 0,2x SSC with 0,1% SDS in comparison to stringent washing conditions as e.g. 60°-30 68°C with 0,1% SDS. Further examples can be found in the references listed above for the stringend hybridization conditions. Usually washing steps are repeated with increasing stringency and length until a useful signal to noise ratio is detected and depend on many factors as the target, e.g. its purity, GC-content, size etc, the probe, e.g. its length, is it a RNA or a DNA probe, salt conditions, washing or hybridisation temperature, washing or hybridisation time etc.

[0406.0.0.0] In another embodiment, the present invention relates to a method for the identification of a gene product conferring an increase in the fine chemical production in a cell, comprising the following steps:

- identifiying nucleic acid molecules of an organism; which can contain a candidate gene encoding a gene product conferring an increase in the fine chemical after expression, which are at least 20%, preferably 25%, more preferably 30%, even more preferred are 35%. 40% or 50%, even more preferred are 60%, 70% or 80%, most preferred are 90% or 95% or more homology to the nucleic acid molecule of the present invention, for example via homology search in a data bank;
  - (b) introducing the candidate nucleic acid molecules in host cells, preferably in a plant cells or microorganisms, appropriate for producing the fine chemical;
  - (c) expressing the identified nucleic acid molecules in the host cells;
  - (d) assaying the the fine chemcial level in the host cells; and
- 15 (e) identifying the nucleic acid molecule and its gene product which expression confers an increase in the the fine chemical level in the host cell after expression compared to the wild type.
  - [0407.0.0.0] The nucleic acid molecules identified can then be used for the production of the fine chemical in the same way as the nucleic acid molecule of the present invention. Accordingly, in one embodiment, the present invention relates to a process for the production of the fine chemical, comprising (a) identifying a nucleic acid molecule according to aforementioned steps (a) to (f) or (a) to (e) and recovering the free or bound fine chemical from a organism having an increased cellular activity of a polypeptide encoded by the isolated nucleic acid molecule compared to a wild type.
- [0408.0.0.0] Furthermore, in one embodiment, the present invention relates to a method for the identification of a compound stimulating production of the fine chemical to said plant comprising:
  - contacting cells which express the polypeptide of the present invention or its mRNA with a candidate compound under cell cultivation conditions;
- 30 b) assaying an increase in expression of said polypeptide or said mRNA;
  - c) comparing the expression level to a standard response made in the absence of said candidate compound; whereby, an increased expression over the standard indicates that the compound is stimulating production of the fine chemical.

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**[0409.0.0.0]** Furthermore, in one embodiment, the present invention relates to a method for the screening for agonists or an antagonist of the activity of the polypeptide of the present invention or used in the process of the present invention, e.g. a polypeptide conferring an increase of the fine chemical in an organism or a part thereof after increasing the activity in an organism or a part thereof, comprising:

- (a) contacting cells, tissues, plants or microorganisms which express the polypeptide according to the invention with a candidate compound or a sample comprising a plurality of compounds under conditions which permit the expression the polypeptide of the present invention or used in the process of the present invention;
- (b) assaying the fine chemical level or the polypeptide expression level in the cell, tissue, plant or microorganism or the media the cell, tissue, plant or microorganisms is cultured or maintained in; and
- (c) identifying a agonist or antagonist by comparing the measured the fine chemical level or polypeptide of the invention or used in the invention expression level with a standard the fine chemical or polypeptide expression level measured in the absence of said candidate compound or a sample comprising said plurality of compounds, whereby an increased level over the standard indicates that the compound or the sample comprising said plurality of compounds is an agonist and a decreased level over the standard indicates that the compound or the sample comprising said plurality of compounds is an antagonist.

**[0410.0.0.0]** Furthermore, in one embodiment, the present invention relates to process for the identification of a compound conferring increased the fine chemical production in a plant or microorganism, comprising the steps:

- culturing a cell or tissue or microorganism or maintaining a plant expressing the polypeptide according to the invention or a nucleic acid molecule encoding said polypeptide and a readout system capable of interacting with the polypeptide under suitable conditions which permit the interaction of the polypeptide with said readout system in the presence of a compound or a sample comprising a
   plurality of compounds and capable of providing a detectable signal in response to the binding of a compound to said polypeptide under conditions which permit the expression of said readout system and the polypeptide of the present invention or used in the process of the invention; and
  - (b) identifying if the compound is an effective agonist by detecting the presence or absence or increase of a signal produced by said readout system.

[0411.0.0.0] The screen for a gene product or an agonist conferring an increase in the fine chemical production can be performed by growth of an organism for example a

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microorganism in the presence of growth reducing amounts of an inhibitor of the synthesis of the fine chemical. Better growth, eg higher dividing rate or high dry mass in comparison to the control under such conditions would identify a gene or gene product or an agonist conferring an increase in fine chemical production.

One can think to screen for increased fine chemical production by for example resistance to a drug blocking the fine chemical synthesis and looking whether this effect is dependent on the protein of the invention e.g. comparing near identical organisms with low and high biological activity of the protein of the invention.

[0413.0.0.0] Said compound may be chemically synthesized or microbiologically produced and/or comprised in, for example, samples, e.g., cell extracts from, e.g., plants, animals or microorganisms, e.g. pathogens. Furthermore, said compound(s) may be known in the art but hitherto not known to be capable of suppressing or activating the polypeptide of the present invention. The reaction mixture may be a cell free extract or may comprise a cell or tissue culture. Suitable set ups for the method of the invention are known to the person skilled in the art and are, for example, generally described in Alberts et al., Molecular Biology of the Cell, third edition (1994), in particular Chapter 17. The compounds may be, e.g., added to the reaction mixture, culture medium, injected into the cell or sprayed onto the plant.

[0414.0.0.0] If a sample containing a compound is identified in the method of the invention, then it is either possible to isolate the compound from the original sample identified as containing the compound capable of activating or increasing the content of the fine chemical in an organism or part thereof, or one can further subdivide the original sample, for example, if it consists of a plurality of different compounds, so as to reduce the number of different substances per sample and repeat the method with the subdivisions of the original sample. Depending on the complexity of the samples, the steps described above can be performed several times, preferably until the sample identified according to the method of the invention only comprises a limited number of or only one substance(s). Preferably said sample comprises substances of similar chemical and/or physical properties, and most preferably said substances are identical. Preferably, the compound identified according to the above-described method or its derivative is further formulated in a form suitable for the application in plant breeding or plant cell and tissue culture.

[0415.0.0.0] The compounds which can be tested and identified according to a method of the invention may be expression libraries, e.g., cDNA expression libraries, peptides, proteins, nucleic acids, antibodies, small organic compounds, hormones, peptidomimetics, PNAs or the like (Milner, Nature Medicine 1 (1995), 879-880; Hupp, Cell 83 (1995), 237-245; Gibbs, Cell 79 (1994), 193-198 and references cited supra). Said compounds can also be functional derivatives or analogues of known inhibitors or activators. Methods for the preparation of chemical derivatives and analogues are well

known to those skilled in the art and are described in, for example, Beilstein, Handbook of Organic Chemistry, Springer edition New York Inc., 175 Fifth Avenue, New York, N.Y. 10010 U.S.A. and Organic Synthesis, Wiley, New York, USA. Furthermore, said derivatives and analogues can be tested for their effects according to methods known in the art. Furthermore, peptidomimetics and/or computer aided design of appropriate derivatives and analogues can be used, for example, according to the methods described above. The cell or tissue that may be employed in the method of the invention preferably is a host cell, plant cell or plant tissue of the invention described in the embodiments hereinbefore.

- 10 [0416.0.0.0] Thus, in a further embodiment the invention relates to a compound obtained or identified according to the method for identifying an agonist of the invention said compound being an agonist of the polypeptide of the present invention or used in the process of the present invention.
- [0417.0.0.0] Accordingly, in one embodiment, the present invention further relates to a compound identified by the method for identifying a compound of the present invention.
  - [0418.0.0.0] Said compound is, for example, a homologous of the polypeptide of the present invention. Homologues of the polypeptid of the present invention can be generated by mutagenesis, e.g., discrete point mutation or truncation of the polypeptide of the present invenion. As used herein, the term "homologue" refers to a variant form of the protein, which acts as an agonist of the activity of the polypeptide of the present invention. An agonist of said protein can retain substantially the same, or a subset, of the biological activities of the polypeptide of the present invention. In particular, said agonist confers the increase of the expression level of the polypeptide of the present invention and/or the expression of said agonist in an organisms or part thereof confers the increase of free and/or bound the fine chemical in the organism or part thereof.

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- [0419.0.0.0] In one embodiment, the invention relates to an antibody specifically recognizing the compound or agonist of the present invention.
- [0420.0.0.0] The invention also relates to a diagnostic composition comprising at least one of the aforementioned nucleic acid molecules, vectors, proteins, antibodies or compounds of the invention and optionally suitable means for detection.
  - **[0421.0.0.0]** The diagnostic composition of the present invention is suitable for the isolation of mRNA from a cell and contacting the mRNA so obtained with a probe comprising a nucleic acid probe as described above under hybridizing conditions, detecting the presence of mRNA hybridized to the probe, and thereby detecting the expression of the protein in the cell. Further methods of detecting the presence of a protein according to the present invention comprise immunotechniques well known in the art, for example enzyme linked immunosorbent assay. Furthermore, it is possible to

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use the nucleic acid molecules according to the invention as molecular markers or primer in plant breeding. Suitable means for detection are well known to a person skilled in the art, e.g. buffers and solutions for hydridization assays, e.g. the aforementioned solutions and buffers, further and means for Southern-, Western-, Northern- etc. —blots, as e.g. described in Sambrook et al. are known.

[0422.0.0.0] In another embodiment, the present invention relates to a kit comprising the nucleic acid molecule, the vector, the host cell, the polypeptide, the antisense nucleic acid, the antibody, plant cell, the plant or plant tissue, the harvestable part, the propagation material and/or the compound or agonist or antagonists identified according to the method of the invention.

[0423.0.0.0] The compounds of the kit of the present invention may be packaged in containers such as vials, optionally with/in buffers and/or solution. If appropriate, one or more of said components might be packaged in one and the same container.

Additionally or alternatively, one or more of said components might be adsorbed to a solid support as, e.g. a nitrocellulose filter, a glas plate, a chip, or a nylon membrane or to the well of a micro titerplate. The kit can be used for any of the herein described methods and embodiments, e.g. for the production of the host cells, transgenic plants, pharmaceutical compositions, detection of homologous sequences, identification of antagonists or agonists, as food or feed or as a supplement thereof, as supplement for the treating of plants, etc.

[0424.0.0.0] Further, the kit can comprise instructions for the use of the kit for any of said embodiments, in particular for the use for producing organisms or part thereof having an increased free or bound the fine chemcial content.

[0425.0.0.0] In one embodiment said kit comprises further a nucleic acid molecule encoding one or more of the aforementioned protein, and/or an antibody, a vector, a host cell, an antisense nucleic acid, a plant cell or plant tissue or a plant.

**[0426.0.0.0]** In a further embodiment, the present invention relates to a method for the production of a agricultural composition providing the nucleic acid molecule, the vector or the polypeptide of the invention or comprising the steps of the method according to the invention for the identification of said compound, agonist or antagonist; and formulating the nucleic acid molecule, the vector or the polypeptide of the invention or the agonist, or compound identified according to the methods or processes of the present invention or with use of the subject matters of the present invention in a form applicable as plant agricultural composition.

[0427.0.0.0] In another embodiment, the present invention relates to a method for the production of a "the fine chemical"-production supporting plant culture composition comprising the steps of the method for of the present invention; and formulating the compound identified in a form acceptable as agricultural composition.

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[0428.0.0.0] Under "acceptable as agricultural composition" is understood, that such a composition is in agreement with the laws regulating the content of fungicides, plant nutrients, herbizides, etc. Preferably such a composition is without any harm for the protected plants and the animals (humans included) fed therewith.

- [0429.0.0.0] The present invention also pertains to several embodiments relating to 5 further uses and methods. The nucleic acid molecule, polypeptide, protein homologues, fusion proteins, primers, vectors, host cells, described herein can be used in one or more of the following methods: identification of plants useful for fine chemical production as mentioned and related organisms; mapping of genomes; identification and localization of sequences of interest; evolutionary studies; determination of regions 10 required for function; modulation of an activity.
- [0430.0.0.0] The nucleic acid molecule of the invention, the vector of the invention or the nucleic acid construct of the invention may also be useful for the production of organisms resistant to inhibitors of the fine chemical e.g. the amino acid production biosynthesis pathways. In particular, the overexpression of the polypeptide of the present invention may protect plants against herbicides, which block the amino acid, in particular the fine chemical, synthesis in said plant. Examples of herbicides blocking the fine chemical synthesis e.g. the amino acid synthesis in plants are for example sulfonylurea and imidazolinone herbicides which catalyze the first step in branched-20 . chain amino acid biosynthesis
  - [0431.0.0.0] Accordingly, the nucleic acid molecules of the present invention have a variety of uses. First, they may be used to identify an organism or a close relative thereof. Also, they may be used to identify the presence thereof or a relative thereof in a mixed population of microorganisms or plants. By probing the extracted genomic DNA of a culture of a unique or mixed population of plants under stringent conditions with a probe spanning a region of the gene of the present invention which is unique to this, one can ascertain whether the present invention has been used or whether it or a close relative is present.
- [0432.0.0.0] Further, the nucleic acid molecule of the invention may be sufficiently homologous to the sequences of related species such that these nucleic acid 30 molecules may serve as markers for the construction of a genomic map in related organism.
  - [0433.0.0.0] Accordingly, the present invention relates to a method for breeding plants for the production of the fine chemical, comprising
- providing a first plant variety produced according to the process of the invention 35 (a) preferably (over)expressing the nucleic acid molecule of the invention;
  - crossing the first plant variety with a second plant variety; and (b)

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- (c) selecting the offspring plants which overproduce the fine chemical by means of analysis the distribution of a molecular marker in the offspring representing the first plant variety and its capability to (over)produce the fine chemical.
- [0434.0.0.0] Details about the use of molecular markers in breeding can be found in Kumar et al., 1999 (Biotech Adv., 17:143-182) and Peleman and van der Voort 2003 (Trends Plant Sci. 2003 Jul;8(7):330-334). The molecular marker can e.g. relate to the nucleic acid molecule of the invention and/or its expression level. Accordingly, the molecular marker can be a probe or a PCR primer set useful for identification of the genomic existence or genomic localisation of the nucleic acid molecule of the invention, e.g. in a Southern blot analysis or a PCR or its expression level, i.g. in a Northern Blot analysis or a quantitative PCR. Accordingly, in one embodiment, the present invention relates to the use of the nucleic acid molecule of the present invention or encoding the polypeptide of the present invention as molecular marker for breeding.
  - [0435.0.0.0] The nucleic acid molecules of the invention are also useful for evolutionary and protein structural studies. By comparing the sequences of the invention or used in the process of the invention to those encoding similar enzymes from other organisms, the evolutionary relatedness of the organisms can be assessed. Similarly, such a comparison permits an assessment of which regions of the sequence are conserved and which are not, which may aid in determining those regions of the protein which are essential for the functioning of the enzyme. This type of determination is of value for protein engineering studies and may give an indication of what the protein can tolerate in terms of mutagenesis without losing function.
  - [0436.0.0.0] Accordingly, the nucleic acid molecule of the invention can be used for the identification of other nucleic acids conferring an increase of the fine chemical after expression.
  - [0437.0.0.0] Further, the nucleic acid molecule of the invention or a fragment of a gene conferring the expression of the polypeptide of the invention, preferably comprising the nucleic acid molecule of the invention, can be used for marker assisted breeding or association mapping of the fine chemical derived traits
- [0438.0.0.0] Accordingly, the nucleic acid of the invention, the polypeptide of the invention, the nucleic acid construct of the invention, the organisms, the host cell, the microorgansims, the plant, plant tissue, plant cell, or the part thereof of the invention, the vector of the invention, the agonist identified with the method of the invention, the nucleic acid molecule identified with the method of the present invention, can be used for the production of the fine chemical or of the fine chemical and one or more other ingredients such as amino acids, in particular Threoinine, Alanine, Glutamin, Glutamic acid, Valine, Aspargine, Phenylalanine, Leucine, Proline, Tryptophan Tyrosine, Valine, Isoleucine and Arginine.

Accordingly, the nucleic acid of the invention, or the nucleic acid molecule identified with the method of the present invention or the complement sequences thereof, the polypeptide of the invention, the nucleic acid construct of the invention, the organisms, the host cell, the microorgansims, the plant, plant tissue, plant cell, or the part thereof of the invention, the vector of the invention, the antagonist identified with the method of the invention, the antibody of the present invention, the antisense molecule of the present invention, can be used for the reduction of the fine chemical in a organism or part thereof, e.g. in a cell.

**[0439.0.0.0]** Further, the nucleic acid of the invention, the polypeptide of the invention, the nucleic acid construct of the invention, the organisms, the host cell, the microorgansims, the plant, plant tissue, plant cell, or the part thereof of the invention, the vector of the invention, the antagonist or the agonist identified with the method of the invention, the antibody of the presen invention, the antisense molecule of the present invention or the nucleic acid molecule identified with the method of the present invention, can be used for the preparation of an agricultural composition.

[0440.0.0.0] Furthermore, the nucleic acid of the invention, the polypeptide of the invention, the nucleic acid construct of the invention, the organisms, the host cell, the microorgansims, the plant, plant tissue, plant cell, or the part thereof of the invention, the vector of the invention, antagonist or the agonist identified with the method of the invention, the antibody of the presen invention, the antisense molecule of the present invention or the nucleic acid molecule identified with the method the present invention, can be used for the identification and production of compounds capable of conferring a modulation of the fine chemical levels in an organism or parts thereof, preferably to identify and produce compounds conferring an increase of the fine chemical levels in an organism or parts thereof, if said identified compound is applied to the organism or part thereof, i.e. as part of its food, or in the growing or culture media.

[0441.0.0.0] These and other embodiments are disclosed and encompassed by the description and examples of the present invention. Further literature concerning any one of the methods, uses and compounds to be employed in accordance with the present invention may be retrieved from public libraries, using for example electronic devices. For example the public database "Medline" may be utilized which is available on the Internet, for example under hftp://www.ncbi.nlm.nih.gov/PubMed/medline.html. Further databases and addresses, such as hftp://www.ncbi.nlm.nih.gov/, hftp://www.infobiogen. fr/, hftp://www.fmi.ch/biology/research-tools.html, hftp://www.tigr.org/, are known to the person skilled in the art and can also be obtained using, e.g., hftp://www.lycos.com. An overview of patent information in biotechnology and a survey of relevant sources of patent information useful for retrospective searching and for current awareness are given in Berks, TIBTECH 12 (1994), 352-364.

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[0442.0.0.0] Table 1 gives an overview about the fine chemicals produced by SEQ ID NO: 1 of the present invention.

Table 1: Fine chemicals produced with SEQ ID NO: 1 (YNL090W)

Metabolite	Method	Min	Max
Tryptophane	LC	1,26	4,39
Proline	LC	1,73	6,29
Arginine	LC	1,54	4,23
Raffinose	LC	2,57	16,05
Ferulic Acid	LC	1,40	2,41
Phenylalanine	LC	1,34	2,75
Tyrosine	LC	1,44	2,55
gamma+beta-Tocopherol	LC	0,36	0,66
Cerotic Acid (C26:0)	GC	1,41	3,78
Lignoceric Acid (C24:0)	GC	1,34	2,14
Alanine	GC ·	1,21	1,57
Glycine	GC	1,46	1,67
Threonine	GC	1,21	2,02
Putrescine	GC	0,18	0,42
Serine	GC	1,29	1,96
Valine	GC	1,20	2,31
Isoleucine	GC	1,30	4,35
Leucine	GC	1,51	5,01
Sinapic Acid	GC	1,28	2,08
3,4-Dihydroxyphenylalanine		1,37	1,87
(=DOPA)	GC	1,07	1,07
Stearic Acid (C18:0)	GC	1,16	2,13
beta-Carotene	LC	1,77	2,68

Column 1 shows the metabolite produced. Column 2 mirrors the analytic method and column 3 and 4 shows the minimum and maximum production of the respective fine chemical as x-fold.

[0443.0.0.0] The present invention is illustrated by the examples, which follow. The present examples illustrate the basic invention without being intended as limiting the subject of the invention. The content of all of the references, patent applications, patents and published patent applications cited in the present patent application is herewith incorporated by reference.

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[0444.0.0.0] Examples

[0445.0.0.0] Example 1: Cloning SEQ ID NO: 1 in Escherichia coli

[0446.0.0.0] SEQ ID NO: 1 was cloned into the plasmids pBR322 (Sutcliffe, J.G. (1979) Proc. Natl Acad. Sci. USA, 75: 3737-3741); pACYC177 (Change & Cohen (1978) J. Bacteriol. 134: 1141-1156); plasmids of the pBS series (pBSSK+, pBSSK-and others; Stratagene, LaJolla, USA) or cosmids such as SuperCos1 (Stratagene, LaJolla, USA) or Lorist6 (Gibson, T.J. Rosenthal, A., and Waterson, R.H. (1987) Gene 53: 283-286) for expression in E. coli using known, well-established procedures (see, for example, Sambrook, J. et al. (1989) "Molecular Cloning: A Laboratory Manual". Cold Spring Harbor Laboratory Press or Ausubel, F.M. et al. (1994) "Current Protocols in Molecular Biology", John Wiley & Sons).

[0447.0.0.0] Example 2: DNA sequencing and computerized functional analysis

[0448.0.0.0] The DNA was sequenced by standard procedures, in particular the chain determination method, using ABI377 sequencers (see, for example, Fleischman, R.D. et al. (1995) "Whole-genome Random Sequencing and Assembly of Haemophilus Influenzae Rd., Science 269; 496-512)".

[0449.0.0.0] Example 3: In-vivo mutagenesis

[0450.0.0.0] An *in vivo* mutagenesis of Corynebacterium glutamicum for the production of amino acids can be carried out by passing a plasmid DNA (or another vector DNA) through E. coli and other microorganisms (for example Bacillus spp. or yeasts such as Saccharomyces cerevisiae), which are not capable of maintaining the integrity of its genetic information. Usual mutator strains have mutations in the genes for the DNA repair system [for example mutHLS, mutD, mutT and the like; for comparison, see Rupp, W.D. (1996) DNA repair mechanisms in Escherichia coli and Salmonella, pp. 2277-2294, ASM: Washington]. The skilled worker knows these strains. The use of these strains is illustrated for example in Greener, A. and Callahan, M. (1994) Strategies 7; 32-34.

[0451.0.0.0] Example 4: DNA transfer between Escherichia coli and Corynebacterium glutamicum

[0452.0.0.0] Several Corynebacterium and Brevibacterium species comprise endogenous plasmids (such as, for example, pHM1519 or pBL1), which replicate autonomously (for a review, see, for example, Martin, J.F. et al. (1987) Biotechnology 5: 137-146). Shuttle vectors for Escherichia coli and Corynebacterium glutamicum can be constructed easily using standard vectors for E. coli (Sambrook, J. et al., (1989),
 "Molecular Cloning: A Laboratory Manual", Cold Spring Harbor Laboratory Press or Ausubel, F.M. et al. (1994) "Current Protocols in Molecular Biology", John Wiley &

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Sons), which have a replication origin for, and suitable marker from, Corynebacterium glutamicum added. Such replication origins are preferably taken from endogenous plasmids, which have been isolated from Corynebacterium and Brevibacterium species. Genes, which are used in particular as transformation markers for these species are genes for kanamycin resistance (such as those which originate from the Tn5 or Tn-903 transposon) or for chloramphenicol resistance (Winnacker, E.L. (1987) "From Genes to Clones - Introduction to Gene Technology, VCH, Weinheim). There are many examples in the literature of the preparation of a large multiplicity of shuttle vectors which are replicated in E. coli and C. glutamicum and which can be used for various purposes including the overexpression of genes (see, for example, Yoshihama, M. et al. (1985) J. Bacteriol. 162: 591-597, Martin, J.F. et al., (1987) Biotechnology, 5: 137-146 and Eikmanns, B.J. et al. (1992) Gene 102: 93-98). Suitable vectors which replicate in coryneform bacteria are for example, pZ1 (Menkel et al., Appl. Environ. Microbiol., 64, 1989: 549 - 554) pEkEx1 (Eikmanns et al., Gene 102, 1991: 93 - 98) or pHS2-1 (Sonnen et al, Gene 107, 1991: 69 - 74). These vectors are based on the cryptic plasmids pHM1519, pBL1 or pGA1. Other plasmid vectors such as, for example, those based on pCG4 (US 4,489,160), pNG2 (Serwold-Davis et al., FEMS Microbiol. Lett., 66, 1990: 119 - 124) or pAG1 (US 5,158,891) can be used in the same manner.

[0453.0.0.0] Using standard methods, it is possible to clone a gene of interest into one of the above-described shuttle vectors and to introduce such hybrid vectors into Corynebacterium glutamicum strains. The transformation of C. glutamicum can be achieved by protoplast transformation (Kastsumata, R. et al., (1984) J. Bacteriol. 159, 306-311), electroporation (Liebl, E. et al., (1989) FEMS Microbiol. Letters, 53: 399-303) and in those cases where specific vectors are used also by conjugation (such as, for example, described in Schäfer, A., et al. (1990) J. Bacteriol. 172: 1663-1666). Likewise, it is possible to transfer the shuttle vectors for C. glutamicum to E. coli by preparing plasmid DNA from C. glutamicum (using standard methods known in the art) and transforming it into E. coli. This transformation step can be carried out using standard methods, but preferably using a Mcr-deficient E. coli strain, such as NM522 (Gough & Murray (1983) J. Mol. Biol. 166: 1-19).

[0454.0.0.0] If the transformed sequence(s) is/are to be integrated advantageously into the genome of the coryneform bacteria, standard techniques known to the skilled worker also exist for this purpose. Examples, which are used for this purpose are plasmid vectors as they have been described by Remscheid et al. (Appl. Environ. Microbiol., 60, 1994: 126–132) for the duplication and amplification of the hom-thrB operon. In this method, the complete gene is cloned into a plasmid vector, which is capable of replication in a host such as E. coli, but not in C. glutamicum. Suitable vectors are, for example, pSUP301 (Simon et al., Bio/Technology 1, 1983: 784–791), pKIBmob or pK19mob (Schäfer et al., Gene 145, 1994: 69–73), pGEM-T (Promega Corp., Madison, WI, USA), pCR2.1-TOPO (Schuman, J. Biol. Chem., 269, 1994:

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32678–32684, US 5,487,993), pCR<sup>®</sup>Blunt (Invitrogen, Groningen, the Netherlands) or pEM1 (Schrumpf et al., J. Bacteriol., 173, 1991: 4510–4516).

[0455.0.0.0] Example 5: Determining the expression of the mutant/transgenic protein

[0456.0.0.0] The observations of the acivity of a mutated, or transgenic, protein in a 5 transformed host cell are based on the fact that the protein is expressed in a similar manner and in a similar quantity as the wild-type protein. A suitable method for determining the transcription quantity of the mutant, or transgenic, gene (a sign for the amount of mRNA which is available for the translation of the gene product) is to carry out a Northern blot (see, for example, Ausubel et al., (1988) Current Protocols in 10 Molecular Biology, Wiley: New York), where a primer which is designed in such a way that it binds to the gene of interest is provided with a detectable marker (usually a radioactive or chemiluminescent marker) so that, when the total RNA of a culture of the organism is extracted, separated on a gel, applied to a stable matrix and incubated with 15 this probe, the binding and quantity of the binding of the probe indicates the presence and also the amount of mRNA for this gene. Another method is a quantitative PCR. This information detects the extent to which the gene has been transcribed. Total cell RNA can be isolated from Corynebacterium glutamicum by a variety of methods, which are known in the art, as described in Bormann, E.R. et al., (1992) Mol. Microbiol. 6: 20 317-326.

[0457.0.0.0] Standard techniques, such as Western blot, may be employed to determine the presence or relative amount of protein translated from this mRNA (see, for example, Ausubel et al. (1988) "Current Protocols in Molecular Biology", Wiley, New York). In this method, total cell proteins are extracted, separated by gel electrophoresis, transferred to a matrix such as nitrocellulose and incubated with a probe, such as an antibody, which binds specifically to the desired protein. This probe is usually provided directly or indirectly with a chemiluminescent or colorimetric marker, which can be detected readily. The presence and the observed amount of marker indicate the presence and the amount of the sought mutant protein in the cell. However, other methods are also known.

[0458.0.0.0] Example 6: Growth of genetically modified Corynebacterium glutamicum: media and culture conditions

[0460.0.0.0] Genetically modified Corynebacteria are grown in synthetic or natural growth media. A number of different growth media for Corynebacteria are known and widely available (Lieb et al. (1989) Appl. Microbiol. Biotechnol. 32: 205-210; von der Osten et al. (1998) Biotechnology Letters 11: 11-16; Patent DE 4 120 867; Liebl (1992) "The Genus Corynebacterium", in: The Procaryotes, Vol. II, Balows, A., et al., Ed. Springer-Verlag).

[0461.0.0.0] Said media which can be used according to the invention usually consist of one or more carbon sources, nitrogen sources, inorganic salts, vitamins and trace elements. Preferred carbon sources are sugars such as mono-, di- or polysaccharides. Examples of very good carbon sources are glucose, fructose, mannose, galactose, ribose, sorbose, ribulose, lactose, maltose, sucrose, raffinose, starch or cellulose. Sugars may also be added to the media via complex compounds such as molasses or other by-products of sugar refining. It may also be advantageous to add mixtures of various carbon sources. Other possible carbon sources are alcohols and/or organic acids such as methanol, ethanol, acetic acid or lactic acid. Nitrogen sources are usually organic or inorganic nitrogen compounds or materials containing said compounds. Examples of nitrogen sources include ammonia gas, aqueous ammonia solutions or ammonium salts such as NH<sub>4</sub>Cl, or (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>, NH<sub>4</sub>OH, nitrates, urea, amino acids or complex nitrogen sources such as cornsteep liquor, soybean flour, soybean protein, yeast extract, meat extract and others. Mixtures of the above nitrogen sources may be used advantageously.

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[0462.0.0.0] Inorganic salt compounds, which may be included in the media comprise the chloride, phosphorus or sulfate salts of calcium, magnesium, sodium, cobalt, molybdenum, potassium, manganese, zinc, copper and iron. Chelating agents may be added to the medium in order to keep the metal ions in solution. Particularly suitable chelating agents include dihydroxyphenols such as catechol or protocatechulate or organic acids such as citric acid. The media usually also contain other growth factors such as vitamins or growth promoters, which include, for example, biotin, riboflavin, thiamine, folic acid, nicotinic acid, panthothenate and pyridoxine. Growth factors and salts are frequently derived from complex media components such as yeast extract, molasses, cornsteep liquor and the like. The exact composition of the compounds used in the media depends heavily on the particular experiment and is decided upon individually for each specific case. Information on the optimization of media can be found in the textbook "Applied Microbiol. Physiology, A Practical Approach" (Ed. P.M. Rhodes, P.F. Stanbury, IRL Press (1997) S. 53-73, ISBN 0 19 963577 3). Growth media can also be obtained from commercial suppliers, for example Standard 1 (Merck) or BHI (Brain heart infusion, DIFCO) and the like.

[0463.0.0.0] All media components are sterilized, either by heat (20 min at 1.5 bar und 121°C) or by filter sterilization. The components may be sterilized either together or, if required, separately. All media components may be present at the start of the cultivation or added continuously or batchwise, as desired.

[0464.0.0.0] The culture conditions are defined separately for each experiment. The temperature is normally between 15°C and 45°C and may be kept constant or may be altered during the experiment. The pH of the medium should be in the range from 5 to 8.5, preferably around 7.0, and can be maintained by adding buffers to the media. An example of a buffer for this purpose is a potassium phosphate buffer. Synthetic buffers

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such as MOPS, HEPES, ACES and the like may be used as an alternative or simultaneously. The culture pH value may also be kept constant during the culture period by addition of, for example, NaOH or NH<sub>4</sub>OH. If complex media components such as yeast extract are used, additional buffers are required less since many complex compounds have a high buffer capacity. When using a fermenter for the culture of microorganisms, the pH value can also be regulated using gaseous ammonia.

[0465.0.0.0] The incubation period is generally in a range of from several hours to several days. This time period is selected in such a way that the maximum amount of product accumulates in the fermentation broth. The growth experiments, which are disclosed can be carried out in a multiplicity of containers such as microtiter plates, glass tubes, glass flasks or glass or metal fermenters of various sizes. To screen a large number of clones, the microorganisms should be grown in microtiter plates, glass tubes or shake flasks, either using simple flasks or baffle flasks. 100 ml shake flasks filled with 10% (based on the volume) of the growth medium required are preferably used. The flasks should be shaken on an orbital shaker (amplitude 25 mm) at a rate ranging from 100 to 300 rpm. Evaporation losses can be reduced by maintaining a humid atmosphere; as an alternative, a mathematical correction should be carried out for the evaporation losses.

[0466.0.0.0] If genetically modified clones are examined, an unmodified control clone, or a control clone, which contains the basic plasmid without insertion, should also be included in the tests. If a transgenic sequence is expressed, a control clone should advantageously again be included in these tests. The medium is advantageously inoculated to an OD600 of 0.5 to 1.5 using cells which have been grown on agar plates, such as CM plates (10 g/l glucose, 2.5 g/l NaCl, 2 g/l urea, 10 g/l polypeptone, 5 g/l yeast extract, 5 g/l meat extract, 22 g/l agar, pH value 6.8 established with 2M NaOH), which have been incubated at 30°C. The media are inoculated either by introducing a saline solution of C. glutamicum cells from CM plates or by addition of a liquid preculture of this bacterium.

30 **[0467.0.0.0]** Example 7: In-vitro analysis of the function of the proteins encoded by the transformed sequences

[0468.0.0.0] The determination of the activities and kinetic parameters of enzymes is well known in the art. Experiments for determining the activity of a specific modified enzyme must be adapted to the specific activity of the wild-enzyme type, which is well within the capabilities of the skilled worker. Overviews of enzymes in general and specific details regarding the structure, kinetics, principles, methods, applications and examples for the determination of many enzyme activities can be found for example in the following literature: Dixon, M., and Webb, E.C: (1979) Enzymes, Longmans, London; Fersht (1985) Enzyme Structure and Mechanism, Freeman, New York; Walsh

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(1979) Enzymatic Reaction Mechanisms. Freeman, San Francisco; Price, N.C., Stevens, L. (1982) Fundamentals of Enzymology. Oxford Univ. Press: Oxford; Boyer, P.D: Ed. (1983) The Enzymes, 3rd Ed. Academic Press, New York; Bisswanger, H. (1994) Enzymkinetik, 2nd Ed. VCH, Weinheim (ISBN 3527300325); Bergmeyer, H.U., Bergmeyer, J., Graßl, M. Ed. (1983-1986) Methods of Enzymatic Analysis, 3rd Ed. Vol. I-XII, Verlag Chemie: Weinheim; and Ullmann's Encyclopedia of Industrial Chemistry (1987) Vol. A9, "Enzymes", VCH, Weinheim, pp. 352-363.

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[0469.0.0.0] Example 8: Analysis of the effect of the nucleic acid molecule on the production of the amino acids

[0470.0.0.0] The effect of the genetic modification in C. glutamicum on the production of an amino acid can be determined by growing the modified microorganisms under suitable conditions (such as those described above) and analyzing the medium and/or the cellular components for the increased production of the amino acid. Such analytical techniques are well known to the skilled worker and encompass spectroscopy, thin-15 layer chromatography, various types of staining methods, enzymatic and microbiological methods and analytical chromatography such as high-performance liquid chromatography (see, for example, Ullman, Encyclopedia of Industrial Chemistry, Vol. A2, pp. 89-90 and pp. 443-613, VCH: Weinheim (1985); Fallon, A., et al., (1987) "Applications of HPLC in Biochemistry" in: Laboratory Techniques in Biochemistry and 20 Molecular Biology, Vol. 17; Rehm et al. (1993) Biotechnology, Vol. 3, Chapter III: "Product recovery and purification", pp. 469-714, VCH: Weinheim; Belter, P.A. et al. (1988) Bioseparations: downstream processing for Biotechnology, John Wiley and Sons; Kennedy, J.F. and Cabral, J.M.S. (1992) Recovery processes for biological Materials, John Wiley and Sons; Shaeiwitz, J.A. and Henry, J.D. (1988) Biochemical 25 Separations, in Ullmann's Encyclopedia of Industrial Chemistry, Vol. B3; chapter 11, pp. 1-27, VCH: Weinheim; and Dechow, F.J. (1989) Separation and purification techniques in biotechnology, Noyes Publications).

[0471.0.0.0] In addition to the determination of the fermentation end product, other components of the metabolic pathways which are used for the production of the desired compound, such as intermediates and by-products, may also be analyzed in order to determine the total productivity of the organism, the yield and/or production efficiency of the compound. The analytical methods encompass determining the amounts of nutrients in the medium (for example sugars, hydrocarbons, nitrogen sources, phosphate and other ions), determining biomass composition and growth, analyzing the production of ordinary metabolites from biosynthetic pathways and measuring gases generated during the fermentation. Standard methods for these are described in Applied Microbial Physiology; A Practical Approach, P.M. Rhodes and P.F. Stanbury, Ed. IRL Press, pp. 103-129; 131-163 and 165-192 (ISBN: 0199635773) and the references cited therein.

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[0472.0.0.0] Example 9: Purification of the amino acid

[0473.0.0.0] The amino acid can be recovered from cells or from the supernatant of the above-described culture by a variety of methods known in the art. For example, the culture supernatant is recovered first. To this end, the cells are harvested from the culture by slow centrifugation. Cells can generally be disrupted or lysed by standard techniques such as mechanical force or sonication. The cell debris is removed by centrifugation and the supernatant fraction, if appropriate together with the culture supernatant, is used for the further purification of the amino acid. However, it is also possible to process the supernatant alone if the amino acid is present in the supernatant in sufficiently high a concentration. In this case, the amino acid, or the amino acid mixture, can be purified further for example via extraction and/or salt precipitation or via ion-exchange chromatography.

[0474.0.0.0] If required and desired, further chromatography steps with a suitable resin may follow, the amino acid, but not many contaminants in the sample, being retained on the chromatography resin or the contaminants, but not the sample with the product (amino acid), being retained on the resin. If necessary, these chromatography steps may be repeated, using identical or other chromatography resins. The skilled worker is familiar with the selection of suitable chromatography resin and the most effective use for a particular molecule to be purified. The purified product can be concentrated by filtration or ultrafiltration and stored at a temperature at which maximum product stability is ensured. Many purification methods, which are not limited to the above purification method are known in the art. They are described, for example, in Bailey, J.E. & Ollis, D.F. Biochemical Engineering Fundamentals, McGraw-Hill: New York (1986).

[0475.0.0.0] Identity and purity of the amino acid isolated can be determined by standard techniques of the art. They encompass high-performance liquid chromatography (HPLC), spectroscopic methods, mass spectrometry (MS), staining methods, thin-layer chromatography, NIRS, enzyme assay or microbiological assays. These analytical methods are compiled in: Patek et al. (1994) Appl. Environ. Microbiol.
60: 133-140; Malakhova et al. (1996) Biotekhnologiya 11: 27-32; and Schmidt et al. (1998) Bioprocess Engineer. 19: 67-70. Ulmann's Encyclopedia of Industrial Chemistry (1996) Vol. A27, VCH: Weinheim, pp. 89-90, pp. 521-540, pp. 540-547, pp. 559-566, 575-581 and pp. 581-587; Michal, G (1999) Biochemical Pathways: An Atlas of Biochemistry and Molecular Biology, John Wiley and Sons; Fallon, A. et al. (1987)
Applications of HPLC in Biochemistry in: Laboratory Techniques in Biochemistry and Molecular Biology, Vol. 17.

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[0476.0.0.0] Example 10: Cloning SEQ ID NO: 1 for the expression in plants

[0477.0.0.0] Unless otherwise specified, standard methods as described in Sambrook et al., Molecular Cloning: A laboratory manual, Cold Spring Harbor 1989, Cold Spring Harbor Laboratory Press are used.

5 [0478.0.0.0] SEQ ID NO: 1 is amplified by PCR as described in the protocol of the Pfu Turbo or DNA Herculase polymerase (Stratagene).

[0479.0.0.0] The composition for the protocol of the *Pfu* Turbo DNA polymerase was as follows: 1x PCR buffer (Stratagene), 0.2 mM of each dNTP, 100 ng genomic DNA of *Saccharomyces cerevisiae* (strain S288C; Research Genetics, Inc., now Invitrogen) or *Escherichia coli* (strain MG1655; *E.coli* Genetic Stock Center), 50 pmol forward primer, 50 pmol reverse primer, 2.5 u *Pfu* Turbo DNA polymerase. The amplification cycles were as follows:

1 cycle of 3 minutes at 94-95°C, followed by 25-36 cycles of in each case 1 minute at 95°C or 30 seconds at 94°C, 45 seconds at 50°C, 30 seconds at 50°C or 30 seconds at 55°C and 210-480 seconds at 72°C, followed by 1 cycle of 8 minutes at 72°C, then 4°C.

[0480.0.0.0] The composition for the protocol of the Herculase polymerase was as follows: 1x PCR buffer (Stratagene), 0.2 mM of each dNTP, 100 ng genomic DNA of Saccharomyces cerevisiae (strain S288C; Research Genetics, Inc., now Invitrogen) or Escherichia coli (strain MG1655; E.coli Genetic Stock Center), 50 pmol forward primer, 50 pmol reverse primer, 2.5 u Herculase polymerase. The amplification cycles were as follows:

[0481.0.0.0] 1 cycle of 2-3 minutes at 94°C, followed by 25-30 cycles of in each case 30 seconds at 94°C, 30 seconds at 55-60°C and 5-10 minutes at 72°C, followed by 1 cycle of 10 minutes at 72°C, then 4°C.

[0482.0.0.0] The following primer sequences were selected for the gene SEQ ID NO: 1:

- i) forward primer (SEQ ID NO: 53)5'-ATGTCTGAAAAGGCCGTTAGAAGG-3'
- 30 ii) reverse primer (SEQ ID NO: 54)
  5'-TTATAAAATTATGCAACAGTTAGCCC-3'

[0483.0.0.0] Thereafter, the amplificate was purified over QIAquick columns following the standard protocol (Qiagen).

- **[0484.0.0.0]** For the cloning of PCR-products, produced by *Pfu* Turbo DNA polymerase, the vector DNA (30 ng) was restricted with *Smal* following the standard protocol (MBI Fermentas) and stopped by addition of high-salt buffer. The restricted vector fragments were purified via Nucleobond columns using the standard protocol (Macherey-Nagel). Thereafter, the linearized vector was dephosphorylated following the standard protocol (MBI Fermentas).
- **[0485.0.0.0]** The PCR-products, produced by *Pfu* Turbo DNA polymerase, were directly cloned into the processed binary vector.
- [0486.0.0.0] The DNA termini of the PCR-products, produced by Herculase DNA polymerase, were blunted in a second synthesis reaction using *Pfu* Turbo DNA polymerase. The composition for the protocol of the blunting the DNA-termini was as follows: 0.2 mM blunting dTTP and 1.25 u *Pfu* Turbo DNA polymerase. The reaction was incubated at 72°C for 30 minutes. Then the PCR-products were cloned into the processed vector as well.
- [0487.0.0.0] A binary vector comprising a selection cassette (promoter, selection marker, terminator) and an expression cassette with promoter, cloning cassette and terminator sequence between the T-DNA border sequences was used. In addition to those within the cloning cassette, the binary vector has no *Smal* cleavage site. Binary vectors which can be used are known to the skilled worker, an overview of binary vectors and their use can be found in Hellens, R., Mullineaux, P. and Klee H., [(2000) "A guide to *Agrobacterium* binary vectors", Trends in Plant Science, Vol. 5 No.10, 446–451. Depending on the vector used, cloning may advantageously also be carried out via other restriction enzymes. Suitable advantageous cleavage sites can be added to the ORF by using suitable primers for the PCR amplification.
- 25 **[0488.0.0.0]** Approximately 30 ng of prepared vector and a defined amount of prepared amplificate were mixed and ligated by addition of ligase.
  - [0489.0.0.0] The ligated vectors were transformed in the same reaction vessel by addition of competent *E. coli* cells (strain DH5alpha) and incubation for 20 minutes at 1°C followed by a heat shock for 90 seconds at 42°C and cooling to 4°C. Then, complete medium (SOC) was added and the mixture was incubated for 45 minutes at 37°C. The entire mixture was subsequently plated onto an agar plate with antibiotics (selected as a function of the binary vector used) and incubated overnight at 37°C.
- [0490.0.0.0] The outcome of the cloning step was verified by amplification with the aid of primers which bind upstream and downstream of the integration site, thus allowing the amplification of the insertion. In addition combinations of the above mentioned gene specific primers and upstream and downstream primers were used in PCR reactions to identify clones with the correct insert orientation. The amplifications were carried as described in the protocol of *Taq* DNA polymerase (Gibco-BRL).

[0491.0.0.0] The amplification cycles were as follows: 1 cycle of 5 minutes at 94°C, followed by 35 cycles of in each case 15 seconds at 94°C, 15 seconds at 50-66°C and 5 minutes at 72°C, followed by 1 cycle of 10 minutes at 72°C, then 4°C.

[0492.0.0.0] Several colonies were checked, but only one colony for which a PCR product of the expected size was detected was used in the following steps.

[0493.0.0.0] A portion of this positive colony was transferred into a reaction vessel filled with complete medium (LB) and incubated overnight at 37°C. The LB medium contained an antibiotic chosen to suit the binary vector (see above) used and the resistance gene present therein in order to select the clone.

10 **[0494.0.0.0]** The plasmid preparation was carried out as specified in the Qiaprep standard protocol (Qiagen).

[0495.0.0.0] Example 11: Generation of transgenic plants which express SEQ ID NO: 1

- [0496.0.0.0] 1 ng of the plasmid DNA isolated was transformed by electroporation into competent cells of Agrobacterium tumefaciens, of strain GV 3101 pMP90 (Koncz and Schell, Mol. Gen. Gent. 204, 383-396, 1986). The choice of the agrobacterial strain depends on the choice of the binary vector. An overview of possible strains and their properties is found in Hellens, R., Mullineaux, P. and Klee H., (2000) "A guide to Agrobacterium binary vectors, Trends in Plant Science, Vol. 5 No.10, 446-451.
- Thereafter, complete medium (YEP) was added and the mixture was transferred into a fresh reaction vessel for 3 hours at 28°C. Thereafter, all of the reaction mixture was plated onto YEP agar plates supplemented with the respective antibiotics, for example rifampicin and gentamycin for GV3101 pMP90, and a further antibiotic for the selection onto the binary vector, was plated, and incubated for 48 hours at 28°C.
- 25 [0497.0.0.0] The agrobacteria generated in Example 10, which contains the plasmid construct were then used for the transformation of plants.

[0498.0.0.0] A colony was picked from the agar plate with the aid of a pipette tip and taken up in 3 ml of liquid TB medium, which also contained suitable antibiotics, depending on the agrobacterial strain and the binary plasmid. The preculture was grown for 48 hours at 28°C and 120 rpm.

[0499.0.0.0] 400 ml of LB medium containing the same antibiotics as above were used for the main culture. The preculture was transferred into the main culture. It was grown for 18 hours at 28°C and 120 rpm. After centrifugation at 4 000 rpm, the pellet was resuspended in infiltration medium (MS medium, 10% sucrose).

[0500.0.0.0] In order to grow the plants for the transformation, dishes (Piki Saat 80, green, provided with a screen bottom,  $30 \times 20 \times 4.5$  cm, from Wiesauplast,

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Kunststofftechnik, Germany) were half-filled with a GS 90 substrate (standard soil, Werkverband E.V., Germany). The dishes were watered overnight with 0.05% Proplant solution (Chimac-Apriphar, Belgium). *Arabidopsis thaliana* C24 seeds (Nottingham Arabidopsis Stock Centre, UK; NASC Stock N906) were scattered over the dish, approximately 1 000 seeds per dish. The dishes were covered with a hood and placed in the stratification facility (8 h, 110 μ μmol/m²/s-¹, 22°C; 16 h, dark, 6°C). After 5 days, the dishes were placed into the short-day controlled environment chamber (8 h 130 μmol/m²/s-¹, 22°C; 16 h, dark 20°C), where they remained for approximately 10 days until the first true leaves had formed.

- 10 [0501.0.0.0] The seedlings were transferred into pots containing the same substrate (Teku pots, 7 cm, LC series, manufactured by Pöppelmann GmbH & Co, Germany). Five plants were pricked out into each pot. The pots were then returned into the short-day controlled environment chamber for the plant to continue growing.
- [0502.0.0.0] After 10 days, the plants were transferred into the greenhouse cabinet (supplementary illumination, 16 h, 340 μE, 22°C; 8 h, dark, 20°C), where they were allowed to grow for further 17 days.
  - [0503.0.0.0] For the transformation, 6-week-old Arabidopsis plants which had just started flowering were immersed for 10 seconds into the above-described agrobacterial suspension which had previously been treated with 10 µl Silwett L77 (Crompton S.A., Osi Specialties, Switzerland). The method in question is described in Clough and Bent, 1998 (Clough, JC and Bent, AF. 1998 Floral dip: a simplified method for Agrobacterium-mediated transformation of Arabidopsis thaliana, Plant J. 16:735-743.
  - **[0504.0.0.0]** The plants were subsequently placed for 18 hours into a humid chamber. Thereafter, the pots were returned to the greenhouse for the plants to continue growing. The plants remained in the greenhouse for another 10 weeks until the seeds were ready for harvesting.
  - [0505.0.0.0] Depending on the resistance marker used for the selection of the transformed plantsthe harvested seeds were planted in the greenhouse and subjected to a spray selection or else first sterilized and then grown on agar plates supplemented with the respective selection agent. . In case of BASTA®-resistance, plantlets were sprayed four times at an interval of 2 to 3 days with 0.02 % BASTA® and transformed plants were allowed to set seeds. The seeds of the transgenic *A. thaliana* plants were stored in the freezer (at -20°C).
  - [0506.0.0.0] Example 12: Plant culture for bioanalytical analyses
- [0507.0.0.0] For the bioanalytical analyses of the transgenic plants, the latter were grown uniformly a specific culture facility. To this end the GS-90 substrate as the compost mixture was introduced into the potting machine (Laible System GmbH,

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Singen, Germany) and filled into the pots. Thereafter, 35 pots were combined in one dish and treated with Previour. For the treatment, 25 ml of Previour were taken up in 10 l of tap water. This amount was sufficient for the treatment of approximately 200 pots. The pots were placed into the Previour solution and additionally irrigated overhead with tap water without Previour. They were used within four days.

[0508.0.0.0] For the sowing, the seeds, which had been stored in the refrigerator (at -20°C), were removed from the Eppendorf tubes with the aid of a toothpick and transferred into the pots with the compost. In total, approximately 5 to 12 seeds were distributed in the middle of the pot.

[0509.0.0.0] After the seeds had been sown, the dishes with the pots were covered with matching plastic hood and placed into the stratification chamber for 4 days in the dark at 4°C. The humidity was approximately 90%. After the stratification, the test plants were grown for 22 to 23 days at a 16-h-light, 8-h-dark rhythm at 20°C, an atmospheric humidity of 60% and a CO<sub>2</sub> concentration of approximately 400 ppm. The light sources used were Powerstar HQI-T 250 W/D Daylight lamps from Osram, which generate a light resembling the solar color spectrum with a light intensity of approximately 220 μE/m2/s-1.

[0510.0.0.0] When the plants were 8, 9 and 10 days old, they were subjected to selection for the resistance marker Approximately 1400 pots with transgenic plants were treated with 11 0,015% vol/vol of Basta® (Glufosinate-ammonium) solution in water (Aventis Cropsience, GermanyAfter a further 3 to 4 days, the transgenic, resistant seedlings (plantlets in the 4-leaf stage) could be distinguished clearly from the untransformed plantlets. The nontransgenic seedlings were bleached or dead. The transgenic resistance plants were thinned when they had reached the age of 14 days. The plants, which had grown best in the center of the pot were considered the target plants. All the remaining plants were removed carefully with the aid of metal tweezers and discarded.

[0511.0.0.0] During their growth, the plants received overhead irrigation with distilled water (onto the compost) and bottom irrigation into the placement grooves. Once the grown plants had reached the age of 23 days, they were harvested.

[0512.0.0.0] Example 13: Metabolic analysis of transformed plants

[0513.0.0.0] The modifications identified in accordance with the invention, in the content of above-described metabolites, were identified by the following procedure.

- a) sampling and storage of the samples
- 35 **[0514.0.0.0]** Sampling was performed directly in the controlled-environment chamber. The plants were cut using small laboratory scissors, rapidly weighed on

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laboratory scales, transferred into a pre-cooled extraction sleeve and placed into an aluminum rack cooled by liquid nitrogen. If required, the extraction sleeves can be stored in the freezer at -80°C. The time elapsing between cutting the plant to freezing it in liquid nitrogen amounted to not more than 10 to 20 seconds.

### b) Lyophilization

[0515.0.0.0] During the experiment, care was taken that the plants either remained in the deep-frozen state (temperatures < -40°C) or were freed from water by lyophilization until the first contact with solvents.

[0516.0.0.0] The aluminum rack with the plant samples in the extraction sleeves was placed into the pre-cooled (-40°C) lyophilization facility. The initial temperature during the main drying phase was-35°C and the pressure was 0.120 mbar. During the drying phase, the parameters were altered following a pressure and temperature program. The final temperature after 12 hours was +30°C and the final pressure was 0.001 to 0.004 mbar. After the vacuum pump and the refrigerating machine had been switched off, the system was flushed with air (dried via a drying tube) or argon.

### c) Extraction

[0517.0.0.0] Immediately after the lyophilization apparatus had been flushed, the extraction sleeves with the lyophilized plant material were transferred into the 5 ml extraction cartridges of the ASE device (Accelerated Solvent Extractor ASE 200 with Solvent Controller and AutoASE software (DIONEX)).

**[0518.0.0.0]** The 24 sample positions of an ASE device (Accelerated Solvent Extractor ASE 200 with Solvent Controller and AutoASE software (DIONEX)) were filled with plant samples, including some samples for testing quality control.

[0519.0.0.0] The polar substances were extracted with approximately 10 ml of methanol/water (80/20, v/v) at T = 70°C and p = 140 bar, 5 minutes heating-up phase, 1 minute static extraction. The more lipophilic substances were extracted with approximately 10 ml of methanol/dichloromethane (40/60, v/v) at T = 70°C and p = 140 bar, 5 minute heating-up phase, 1 minute static extraction. The two solvent mixtures were extracted into the same glass tubes (centrifuge tubes, 50 ml, equipped with screw cap and pierceable septum for the ASE (DIONEX)).

**[0520.0.0.0]** The solution was treated with internal standards: ribitol, L-glycine-2,2-d<sub>2</sub>, L-alanine-2,3,3,3-d<sub>4</sub>, methionine-methyl-d<sub>3</sub>, and  $\alpha$ -methylglucopyranoside and methyl nonadecanoate, methyl undecanoate, methyl tridecanoate, methyl pentadecanoate, methyl nonacosanoate.

35 [0521.0.0.0] The total extract was treated with 8 ml of water. The solid residue of the plant sample and the extraction sleeve were discarded.

[0522.0.0.0] The extract was shaken and then centrifuged for 5 to 10 minutes at at least 1 400 g in order to accelerate phase separation. 1 ml of the supernatant methanol/water phase ("polar phase", colorless) was removed for the further GC analysis, and 1 ml was removed for the LC analysis. The remainder of the methanol/water phase was discarded. 0.5 ml of the organic phase ("lipid phase", dark green) was removed for the further GC analysis and 0.5 ml was removed for the LC analysis. All the portions removed were evaporated to dryness using the IR Dancer infrared vacuum evaporator (Hettich). The maximum temperature during the evaporation process did not exceed 40°C. Pressure in the apparatus was not less than 10 mbar.

d) Processing the lipid phase for the LC/MS or LC/MS/MS analysis

[0523.0.0.0] The lipid extract, which had been evaporated to dryness was taken up in mobile phase. The HPLC was run with gradient elution.

- 15 [0524.0.0.0] The polar extract, which had been evaporated to dryness was taken up in mobile phase. The HPLC was run with gradient elution.
  - e) Derivatization of the lipid phase for the GC/MS analysis
- [0525.0.0.0] For the transmethanolysis, a mixture of 140 µl of chloroform, 37 µl of hydrochloric acid (37% by weight HCl in water), 320 µl of methanol and 20 µl of toluene was added to the evaporated extract. The vessel was sealed tightly and heated for 2 hours at 100°C, with shaking. The solution was subsequently evaporated to dryness. The residue was dried completely.
- [0526.0.0.0] The methoximation of the carbonyl groups was carried out by reaction with methoxyamine hydrochloride (5 mg/ml in pyridine, 100 μl for 1.5 hours at 60°C) in a tightly sealed vessel. 20 μl of a solution of odd-numbered, straight-chain fatty acids (solution of each 0.3 mg/mL of fatty acids from 7 to 25 carbon atoms and each 0.6 mg/mL of fatty acids with 27, 29 and 31 carbon atoms in 3/7 (v/v) pyridine/toluene) were added as time standards. Finally, the derivatization with 100 μl of N-methyl-N-(trimethylsilyl)-2,2,2-trifluoroacetamide (MSTFA) was carried out for 30 minutes at 60°C, again in the tightly sealed vessel. The final volume before injection into the GC was 220 μl.
  - f) Derivatization of the polar phase for the GC/MS analysis
- 35 [0527.0.0.0] The methoximation of the carbonyl groups was carried out by reaction with methoxyamine hydrochloride (5 mg/ml in pyridine, 50 μl for 1.5 hours at 60°C) in a

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tightly sealed vessel. 10  $\mu$ l of a solution of odd-numbered, straight-chain fatty acids (solution of each 0.3 mg/mL of fatty acids from 7 to 25 carbon atoms and each 0.6 mg/mL of fatty acids with 27, 29 and 31 carbon atoms in 3/7 (v/v) pyridine/toluene) were added as time standards. Finally, the derivatization with 50  $\mu$ l of N-methyl-N-(trimethylsilyl)-2,2,2-trifluoroacetamide (MSTFA) was carried out for 30 minutes at 60°C, again in the tightly sealed vessel. The final volume before injection into the GC was 110  $\mu$ l.

### g) Analysis of the various plant samples

[0528.0.0.0] The samples were measured in individual series of 20 plant samples each (also referred to as sequences), each sequence containing at least 5 wild-type plants as controls. The peak area of each analyte was divided by the peak area of the respective internal standard. The data were standardized for the fresh weight established for the plant. The values calculated thus were related to the wild-type control group by being divided by the mean of the corresponding data of the wild-type control group of the same sequence. The values obtained were referred to as ratio\_by\_WT, they are comparable between sequences and indicate how much the analyte concentration in the mutant differs in relation to the wild-type control. Appropriate controls were done before to proof that the vector and transformation procedure itself has no significant influence on the metabolic composition of the plants. Therefore the desribed changes in comparison with wildtypes were caused by the introduced genes.

[0529.0.0.0] As an alternative, the amino acids can be detected advantageously via HPLC separation in ethanolic extract as described by Geigenberger et al. (Plant Cell & Environ, 19, 1996: 43–55).

25 The results of the different plant analyses can be seen from the table 1.

[0530.0.0.0] Column 1 in Table 1 shows the amino acid analyzed. Columns 3 and 4 shows the ratio of the analyzed amino acid between the transgenic plants and the wild type; Increase of the metabolites: Max: maximal x-fold (normalised to wild type)-Min: minimal x-fold (normalised to wild type). Decrease of the metabolites: Max: maximal x-fold (normalised to wild type) (minimal decrease), Min: minimal x-fold (normalised to wild type) (maximal decrease). Column 2 indicates the analytical method.

[0531.0.0.0] When the analyses were repeated independently, all results proved to be significant.

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[0532.0.0.0] Example 14a: Engineering ryegrass plants by over-expressing YNL090W, e.g. from Saccharomyces cerevisiae or plants

[0533.0.0.0] Seeds of several different ryegrass varieties can be used as explant sources for transformation, including the commercial variety Gunne available from Svalof Weibull seed company or the variety Affinity. Seeds are surface-sterilized sequentially with 1% Tween-20 for 1 minute, 100 % bleach for 60 minutes, 3 rinses with 5 minutes each with de-ionized and distilled H2O, and then germinated for 3-4 days on moist, sterile filter paper in the dark. Seedlings are further sterilized for 1 minute with 1% Tween-20, 5 minutes with 75% bleach, and rinsed 3 times with ddH<sub>2</sub>O, 5 min each.

[0534.0.0.0] Surface-sterilized seeds are placed on the callus induction medium containing Murashige and Skoog basal salts and vitamins, 20 g/l sucrose, 150 mg/l asparagine, 500 mg/l casein hydrolysate, 3 g/l Phytagel, 10 mg/l BAP, and 5 mg/l dicamba. Plates are incubated in the dark at 25°C for 4 weeks for seed germination and embryogenic callus induction.

[0535.0.0.0] After 4 weeks on the callus induction medium, the shoots and roots of the seedlings are trimmed away, the callus is transferred to fresh media, is maintained in culture for another 4 weeks, and is then transferred to MSO medium in light for 2 weeks. Several pieces of callus (11-17 weeks old) are either strained through a 10 mesh sieve and put onto callus induction medium, or are cultured in 100 ml of liquid ryegrass callus induction media (same medium as for callus induction with agar) in a 250 ml flask. The flask is wrapped in foil and shaken at 175 rpm in the dark at 23°C for 1 week. Sieving the liquid culture with a 40-mesh sieve is collected the cells. The fraction collected on the sieve is plated and is cultured on solid ryegrass callus induction medium for 1 week in the dark at 25°C. The callus is then transferred to and is cultured on MS medium containing 1% sucrose for 2 weeks.

[0536.0.0.0] Transformation can be accomplished with either Agrobacterium or with particle bombardment methods. An expression vector is created containing a constitutive plant promoter and the cDNA of the gene in a pUC vector. The plasmid DNA is prepared from E. coli cells using with Qiagen kit according to manufacturer's instruction. Approximately 2 g of embryogenic callus is spread in the center of a sterile filter paper in a Petri dish. An aliquot of liquid MSO with 10 g/l sucrose is added to the filter paper. Gold particles (1.0 µm in size) are coated with plasmid DNA according to method of Sanford et al., 1993 and are delivered to the embryogenic callus with the following parameters: 500 µg particles and 2 µg DNA per shot, 1300 psi and a target distance of 8.5 cm from stopping plate to plate of callus and 1 shot per plate of callus.

[0537.0.0.0] After the bombardment, calli are transferred back to the fresh callus development medium and maintained in the dark at room temperature for a 1-week

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period. The callus is then transferred to growth conditions in the light at 25 °C to initiate embryo differentiation with the appropriate selection agent, e.g. 250 nM Arsenal, 5 mg/l PPT or 50 mg/L Kanamycin. Shoots resistant to the selection agent are appearing and once rooted are transferred to soil.

[0538.0.0.0] Samples of the primary transgenic plants (T0) are analyzed by PCR to 5 confirm the presence of T-DNA. These results are confirmed by Southern hybridization in which DNA is electrophoresed on a 1% agarose gel and transferred to a positively charged nylon membrane (Roche Diagnostics). The PCR DIG Probe Synthesis Kit (Roche Diagnostics) is used to prepare a digoxigenin-labelled probe by PCR, and used as recommended by the manufacturer. 10

[0539.0.0.0] Transgenic T0 ryegrass plants are propagated vegetatively by excising tillers. The transplanted tillers are maintained in the greenhouse for 2 months until well established. The shoots are defoliated and allowed to grow for 2 weeks.

[0540.0.0.0] Example 14b: Engineering soybean plants by over-expressing YNL090W, e.g. from Saccharomyces cerevisiae or plants

[0541.0.0.0] Soybean can be transformed according to the following modification of the method described in the Texas A&M patent US 5,164,310. Several commercial soybean varieties are amenable to transformation by this method. The cultivar Jack (available from the Illinois Seed Foundation) is commonly used for transformation. Seeds are sterilized by immersion in 70% (v/v) ethanol for 6 min and in 25 % commercial bleach (NaOCl) supplemented with 0.1% (v/v) Tween for 20 min, followed by rinsing 4 times with sterile double distilled water. Removing the radicle, hypocotyl and one cotyledon from each seedling propagates seven-day seedlings. Then, the epicotyl with one cotyledon is transferred to fresh germination media in petri dishes and incubated at 25 °C under a 16-hr photoperiod (approx. 100  $\mu\text{E-m-2s-1}$ ) for three 25 weeks. Axillary nodes (approx. 4 mm in length) are cut from 3 – 4 week-old plants. Axillary nodes are excised and incubated in Agrobacterium LBA4404 culture.

[0542.0.0.0] Many different binary vector systems have been described for plant transformation (e.g. An, G. in Agrobacterium Protocols. Methods in Molecular Biology vol 44, pp 47-62, Gartland KMA and MR Davey eds. Humana Press, Totowa, New Jersey). Many are based on the vector pBIN19 described by Bevan (Nucleic Acid Research. 1984. 12:8711-8721) that includes a plant gene expression cassette flanked by the left and right border sequences from the Ti plasmid of Agrobacterium tumefaciens. A plant gene expression cassette consists of at least two genes - a selection marker gene and a plant promoter regulating the transcription of the cDNA or genomic DNA of the trait gene. Various selection marker genes can be used as described above, including the Arabidopsis gene encoding a mutated acetohydroxy acid synthase (AHAS) enzyme (US patents 57673666 and 6225105). Similarly, various promoters can be used to regulate the trait gene to provide constitutive, developmental, tissue or environmental regulation of gene transcription as described above. In this example, the 34S promoter (GenBank Accession numbers M59930 and X16673) is used to provide constitutive expression of the trait gene.

- [0543.0.0.0] After the co-cultivation treatment, the explants are washed and transferred to selection media supplemented with 500 mg/L timentin. Shoots are excised and placed on a shoot elongation medium. Shoots longer than 1 cm are placed on rooting medium for two to four weeks prior to transplanting to soil.
- [0544.0.0.0] The primary transgenic plants (T0) are analyzed by PCR to confirm the presence of T-DNA. These results are confirmed by Southern hybridization in which DNA is electrophoresed on a 1 % agarose gel and transferred to a positively charged nylon membrane (Roche Diagnostics). The PCR DIG Probe Synthesis Kit (Roche Diagnostics) is used to prepare a digoxigenin-labelled probe by PCR, and is used as recommended by the manufacturer.
- 15 [0545.0.0.0] Example 14c: Engineering corn plants by over-expressing YNL090W, e.g. from Saccharomyces cerevisiae or plants
- [0546.0.0.0] Transformation of maize (Zea Mays L.) is performed with a modification of the method described by Ishida et al. (1996. Nature Biotech 14745-50). Transformation is genotype-dependent in com and only specific genotypes are 20 amenable to transformation and regeneration. The inbred line A188 (University of Minnesota) or hybrids with A188 as a parent are good sources of donor material for transformation (Fromm et al. 1990 Biotech 8:833-839), but other genotypes can be used successfully as well. Ears are harvested from corn plants at approximately 11 days after pollination (DAP) when the length of immature embryos is about 1 to 1.2 mm. Immature embryos are co-cultivated with Agrobacterium tumefaciens that carry 25 "super binary" vectors and transgenic plants are recovered through organogenesis. The super binary vector system of Japan Tobacco is described in WO patents WO94/00977 and WO95/06722. Vectors can be constructed as described. Various selection marker genes can be used including the maize gene encoding a mutated 30 acetohydroxy acid synthase (AHAS) enzyme (US patent 6025541). Similarly, various promoters can be used to regulate the trait gene to provide constitutive, developmental, tissue or environmental regulation of gene transcription. In this example, the 34S promoter (GenBank Accession numbers M59930 and X16673) is used to provide constitutive expression of the trait gene.
- [0547.0.0.0] Excised embryos are grown on callus induction medium, then maize regeneration medium, containing imidazolinone as a selection agent. The Petri plates are incubated in the light at 25 °C for 2-3 weeks, or until shoots develop. The green shoots are transferred from each embryo to maize rooting medium and incubated at 25

°C for 2-3 weeks, until roots develop. The rooted shoots are transplanted to soil in the greenhouse. T1 seeds are produced from plants that exhibit tolerance to the imidazolinone herbicides and which are PCR positive for the transgenes.

[0548.0.0.0] The T1 generation of single locus insertions of the T-DNA can segregate for the transgene in a 3:1 ratio. Those progeny containing one or two copies of the transgene are tolerant of the imidazolinone herbicide. Homozygous T2 plants can exhibited similar phenotypes as the T1 plants. Hybrid plants (F1 progeny) of homozygous transgenic plants and non-transgenic plants can also exhibited increased similar phenotyps.

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10 [0549.0.0.0] Example 14d: Engineering wheat plants by over-expressing YNL090W, e.g. from Saccharomyces cerevisiae or plants

[0550.0.0.0] Transformation of wheat is performed with the method described by Ishida et al. (1996 Nature Biotech. 14745-50). The cultivar Bobwhite (available from CYMMIT, Mexico) is commonly used in transformation. Immature embryos are co-cultivated with Agrobacterium tumefaciens that carry "super binary" vectors, and transgenic plants are recovered through organogenesis. The super binary vector system of Japan Tobacco is described in WO patents WO94/00977 and WO95/06722. Vectors were constructed as described. Various selection marker genes can be used including the maize gene encoding a mutated acetohydroxy acid synthase (AHAS) enzyme (US patent 6025541). Similarly, various promoters can be used to regulate the trait gene to provide constitutive, developmental, tissue or environmental regulation of gene transcription. In this example, the 34S promoter (GenBank Accession numbers M59930 and X16673) can be used to provide constitutive expression of the trait gene.

[0551.0.0.0] After incubation with Agrobacterium, the embryos are grown on callus induction medium, then regeneration medium, containing imidazolinone as a selection agent. The Petri plates are incubated in the light at 25 °C for 2-3 weeks, or until shoots develop. The green shoots are transferred from each embryo to rooting medium and incubated at 25 °C for 2-3 weeks, until roots develop. The rooted shoots are transplanted to soil in the greenhouse. T1 seeds are produced from plants that exhibit tolerance to the imidazolinone herbicides and which are PCR positive for the transgenes.

**[0552.0.0.0]** The T1 generation of single locus insertions of the T-DNA can segregate for the transgene in a 3:1 ratio. Those progeny containing one or two copies of the transgene are tolerant of the imidazolinone herbicide. Homozygous T2 plants exhibited similar phenotypes.

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[0553.0.0.0] Example 14e: Engineering Rapeseed/Canola plants by over-expressing YNL090W, e.g. from Saccharomyces cerevisiae or plants

[0554.0.0.0] Cotyledonary petioles and hypocotyls of 5-6 day-old young seedlings are used as explants for tissue culture and transformed according to Babic et al. (1998, Plant Cell Rep 17: 183-188). The commercial cultivar Westar (Agriculture Canada) is the standard variety used for transformation, but other varieties can be used.

[0555.0.0.0] Agrobacterium tumefaciens LBA4404 containing a binary vector are used for canola transformation. Many different binary vector systems have been described for plant transformation (e.g. An, G. in Agrobacterium Protocols. Methods in Molecular Biology vol 44, pp 47-62, Gartland KMA and MR Davey eds. Humana Press, Totowa, New Jersey). Many are based on the vector pBIN19 described by Bevan (Nucleic Acid Research. 1984. 12:8711-8721) that includes a plant gene expression cassette flanked by the left and right border sequences from the Ti plasmid of Agrobacterium tumefaciens. A plant gene expression cassette consists of at least two genes – a selection marker gene and a plant promoter regulating the transcription of the cDNA or genomic DNA of the trait gene. Various selection marker genes can be used including the Arabidopsis gene encoding a mutated acetohydroxy acid synthase (AHAS) enzyme (US patents 57673666 and 6225105). Similarly, various promoters can be used to regulate the trait gene to provide constitutive, developmental, tissue or environmental regulation of gene transcription. In this example, the 34S promoter (GenBank Accession numbers M59930 and X16673) can be used to provide constitutive expression of the trait gene.

[0556.0.0.0] Canola seeds are surface-sterilized in 70% ethanol for 2 min., and then in 30% Clorox with a drop of Tween-20 for 10 min, followed by three rinses with sterilized distilled water. Seeds are then germinated in vitro 5 days on half strength MS medium without hormones, 1% sucrose, 0.7% Phytagar at 23oC, 16 hr. light. The cotyledon petiole explants with the cotyledon attached are excised from the in vitro seedlings, and are inoculated with Agrobacterium by dipping the cut end of the petiole explant into the bacterial suspension. The explants are then cultured for 2 days on MSBAP-3 medium containing 3 mg/l BAP, 3 % sucrose, 0.7 % Phytagar at 23 °C, 16 hr light. After two days of co-cultivation with Agrobacterium, the petiole explants are transferred to MSBAP-3 medium containing 3 mg/l BAP, cefotaxime, carbenicillin, or timentin (300 mg/l) for 7 days, and then cultured on MSBAP-3 medium with cefotaxime, carbenicillin, or timentin and selection agent until shoot regeneration. When the shoots are 5 – 10 mm in length, they are cut and transferred to shoot elongation medium (MSBAP-0.5, containing 0.5 mg/l BAP). Shoots of about 2 cm in length are transferred to the rooting medium (MSO) for root induction.

[0557.0.0.0] Samples of the primary transgenic plants (T0) are analyzed by PCR to confirm the presence of T-DNA. These results are confirmed by Southern hybridization

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in which DNA is electrophoresed on a 1 % agarose gel and are transferred to a positively charged nylon membrane (Roche Diagnostics). The PCR DIG Probe Synthesis Kit (Roche Diagnostics) is used to prepare a digoxigenin-labelled probe by PCR, and used as recommended by the manufacturer.

5 [0558.0.0.0] Example 14f: Engineering alfalfa plants by over-expressing
YNL090W genes, e.g. from Saccharomyces cerevisiae
or E. coli or plants

[0559.0.0.0] A regenerating clone of alfalfa (Medicago sativa) is transformed using the method of (McKersie et al., 1999 Plant Physiol 119: 839–847). Regeneration and transformation of alfalfa is genotype dependent and therefore a regenerating plant is required. Methods to obtain regenerating plants have been described. For example, these can be selected from the cultivar Rangelander (Agriculture Canada) or any other commercial alfalfa variety as described by Brown DCW and A Atanassov (1985. Plant Cell Tissue Organ Culture 4: 111-112). Alternatively, the RA3 variety (University of Wisconsin) has been selected for use in tissue culture (Walker et al., 1978 Am J Bot 65:654-659).

[0560.0.0.0] Petiole explants are cocultivated with an overnight culture of Agrobacterium tumefaciens C58C1 pMP90 (McKersie et al., 1999 Plant Physiol 119: 839-847) or LBA4404 containing a binary vector. Many different binary vector systems have been described for plant transformation (e.g. An, G. in Agrobacterium Protocols. Methods in Molecular Biology vol 44, pp 47-62, Gartland KMA and MR Davey eds. Humana Press, Totowa, New Jersey). Many are based on the vector pBIN19 described by Bevan (Nucleic Acid Research. 1984. 12:8711-8721) that includes a plant gene expression cassette flanked by the left and right border sequences from the Ti plasmid of Agrobacterium tumefaciens. A plant gene expression cassette consists of at least two genes - a selection marker gene and a plant promoter regulating the transcription of the cDNA or genomic DNA of the trait gene. Various selection marker genes can be used including the Arabidopsis gene encoding a mutated acetohydroxy acid synthase (AHAS) enzyme (US patents 57673666 and 6225105). Similarly, various promoters can be used to regulate the trait gene that provides constitutive, developmental, tissue or environmental regulation of gene transcription. In this example, the 34S promoter (GenBank Accession numbers M59930 and X16673) can be used to provide constitutive expression of the trait gene.

[0561.0.0.0] The explants are cocultivated for 3 d in the dark on SH induction medium containing 288 mg/ L Pro, 53 mg/ L thioproline, 4.35 g/ L K2SO4, and 100 µm acetosyringinone. The explants are washed in half-strength Murashige-Skoog medium (Murashige and Skoog, 1962) and plated on the same SH induction medium without acetosyringinone but with a suitable selection agent and suitable antibiotic to inhibit Agrobacterium growth. After several weeks, somatic embryos are transferred to BOi2Y

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development medium containing no growth regulators, no antibiotics, and 50 g/L sucrose. Somatic embryos are subsequently germinated on half-strength Murashige-Skoog medium. Rooted seedlings are transplanted into pots and grown in a greenhouse.

[0562.0.0.0] The T0 transgenic plants are propagated by node cuttings and rooted in Turface growth medium. The plants are defoliated and grown to a height of about 10 cm (approximately 2 weeks after defoliation).

[0563.0.0.0] Example 14g: Engineering alfalfa plants by over-expressing YLR375W genes, e.g. from Saccharomyces cerevisiae or plants

[0564.0.0.0] A regenerating clone of alfalfa (Medicago sativa) is transformed using the method of (McKersie et al., 1999 Plant Physiol 119: 839–847). Regeneration and transformation of alfalfa is genotype dependent and therefore a regenerating plant is required. Methods to obtain regenerating plants have been described. For example, these can be selected from the cultivar Rangelander (Agriculture Canada) or any other commercial alfalfa variety as described by Brown DCW and A Atanassov (1985. Plant Cell Tissue Organ Culture 4: 111-112). Alternatively, the RA3 variety (University of Wisconsin) has been selected for use in tissue culture (Walker et al., 1978 Am J Bot 65:654-659).

- 20 Petiole explants are cocultivated with an overnight culture of [0565.0.0.0] Agrobacterium tumefaciens C58C1 pMP90 (McKersie et al., 1999 Plant Physiol 119: 839-847) or LBA4404 containing a binary vector. Many different binary vector systems have been described for plant transformation (e.g. An, G. in Agrobacterium Protocols. Methods in Molecular Biology vol 44, pp 47-62, Gartland KMA and MR Davey eds. 25 Humana Press, Totowa, New Jersey). Many are based on the vector pBIN19 described by Bevan (Nucleic Acid Research. 1984. 12:8711-8721) that includes a plant gene expression cassette flanked by the left and right border sequences from the Ti plasmid of Agrobacterium tumefaciens. A plant gene expression cassette consists of at least two genes – a selection marker gene and a plant promoter regulating the transcription 30 of the cDNA or genomic DNA of the trait gene. Various selection marker genes can be used including the Arabidopsis gene encoding a mutated acetohydroxy acid synthase (AHAS) enzyme (US patents 57673666 and 6225105). Similarly, various promoters can be used to regulate the trait gene that provides constitutive, developmental, tissue or environmental regulation of gene transcription. In this example, the 34S promoter 35 (GenBank Accession numbers M59930 and X16673) can be used to provide constitutive expression of the trait gene.
  - [0566.0.0.0] The explants are cocultivated for 3 d in the dark on SH induction medium containing 288 mg/ L Pro, 53 mg/ L thioproline, 4.35 g/ L K2SO4, and 100 µm

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acetosyringinone. The explants are washed in half-strength Murashige-Skoog medium (Murashige and Skoog, 1962) and plated on the same SH induction medium without acetosyringinone but with a suitable selection agent and suitable antibiotic to inhibit Agrobacterium growth. After several weeks, somatic embryos are transferred to BOi2Y development medium containing no growth regulators, no antibiotics, and 50 g/L sucrose. Somatic embryos are subsequently germinated on half-strength Murashige-Skoog medium. Rooted seedlings are transplanted into pots and grown in a greenhouse.

[0567.0.0.0] The T0 transgenic plants are propagated by node cuttings and rooted in Turface growth medium. The plants are defoliated and grown to a height of about 10 cm (approximately 2 weeks after defoliation).

[0568.0.0.0] Equivalents

[0569.0.0.0] Those of ordinary skill in the art will recognize, or will be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the claims.

#### We claim:

- 1. A process for the production of fine chemical, which comprises
- increasing or generating the biological activity represented by a protein as a) depicted in SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 5 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 10 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 15 384, 386, 388, 390, 392 or 394 in a non-human organism, or in one or more parts thereof; and
  - b) growing the organism under conditions which permit the production of the fine chemical in said organism.
- 20 2. A process for the production of fine chemical, comprising the increasing or generating in an organism or a part thereof the expression of at least one nucleic acid molecule comprising a nucleic acid molecule selected from the group consisting of:
- nucleic acid molecule encoding of the polypeptide as depicted in SEQ ID a) NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 25 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 30 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 330, 35 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 or a fragment thereof, which confers an increase in the amount of fine chemical in an organism or a part thereof;

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- nucleic acid molecule comprising of the nucleic acid molecule as depicted in b) SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 5 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 10 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393;
- 15 c) nucleic acid molecule whose sequence can be deduced from a polypeptide sequence encoded by a nucleic acid molecule of (a) or (b) as a result of the degeneracy of the genetic code and conferring an increase in the amount of fine chemical in an organism or a part thereof;
  - d) nucleic acid molecule which encodes a polypeptide which has at least 50% identity with the amino acid sequence of the polypeptide encoded by the nucleic acid molecule of (a) to (c) and conferring an increase in the amount of fine chemical in an organism or a part thereof;
    - e) nucleic acid molecule which hybridizes with a nucleic acid molecule of (a) to (c) under stringent hybridization conditions and conferring an increase in the amount of fine chemical in an organism or a part thereof;
    - f) nucleic acid molecule which encompasses a nucleic acid molecule which is obtained by amplifying nucleic acid molecules from a cDNA library or a genomic library using the primers in SEQ ID NO: 53 or SEQ ID NO: 54 and conferring an increase in the amount of the fine chemical in an organism or a part thereof;
    - g) nucleic acid molecule encoding a polypeptide which is isolated with the aid of monoclonal antibodies against a polypeptide encoded by one of the nucleic acid molecules of (a) to (f) and conferring an increase in the amount of fine chemical in an organism or a part thereof;
- h) nucleic acid molecule encoding a polypeptide comprising the consensus sequence as depicted in SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 397, SEQ ID NO: 398, SEQ ID NO: 399 and/or SEQ ID NO: 400 and conferring an

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increase in the amount of the fine chemical in an organism or a part thereof; and

- nucleic acid molecule which is obtainable by screening a suitable nucleic acid library under stringent hybridization conditions with a probe comprising one of the sequences of the nucleic acid molecule of (a) to (k) or with a fragment thereof having at least 15 nt, preferably 20 nt, 30 nt, 50 nt, 100 nt, 200 nt or 500 nt of the nucleic acid molecule characterized in (a) to (k) and conferring an increase in the amount of the fine chemical in an organism or a part thereof.
- or comprising a sequence which is complementary thereto.
  - 3. The process of claim 1 or 2, comprising recovering of the free or bound fine chemical.
  - 4. The process of any one of claim 1 to 3, comprising the following steps:
  - (a) selecting an organism or a part thereof expressing a polypeptide encoded by the nucleic acid molecule characterized in claim 2;
    - (b) mutagenizing the selected organism or the part thereof;
    - (c) comparing the activity or the expression level of said polypeptide in the mutagenized organism or the part thereof with the activity or the expression of said polypeptide of the selected organisms or the part thereof;
- 20 (d) selecting the mutated organisms or parts thereof, which comprise an increased activity or expression level of said polypeptide compared to the selected organism or the part thereof;
  - (e) optionally, growing and cultivating the organisms or the parts thereof; and
  - (f) recovering, and optionally isolating, the free or bound fine chemical produced by the selected mutated organisms or parts thereof.
  - 5. The process of any one of claims 1 to 4, wherein the activity of said protein or the expression of said nucleic acid molecule is increased or generated transiently or stably.
- 6. An isolated nucleic acid molecule comprising a nucleic acid molecule selected from the group consisting of:
  - (a) nucleic acid molecule encoding of the polypeptide as depicted in SEQ IDNO: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88,

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- (b) nucleic acid molecule comprising of the nucleic acid molecule as depicted in SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 or a fragment thereof, which confers an increase in the amount of fine chemical in an organism or a part thereof;
  - (c) nucleic acid molecule whose sequence can be deduced from a polypeptide sequence encoded by a nucleic acid molecule of (a) or (b) as a result of the degeneracy of the genetic code and conferring an increase in the amount of fine chemical in an organism or a part thereof;
  - (d) nucleic acid molecule which encodes a polypeptide which has at least 50% identity with the amino acid sequence of the polypeptide encoded by the nucleic acid molecule of (a) to (c) and conferring an increase in the amount of fine chemical in an organism or a part thereof;
  - (e) nucleic acid molecule which hybridizes with a nucleic acid molecule of (a) to
     (c) under stringent hybridization conditions and conferring an increase in the amount of fine chemical in an organism or a part thereof;

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- (f) nucleic acid molecule which encompasses a nucleic acid molecule which is obtained by amplifying nucleic acid molecules from a cDNA library or a genomic library using the primers in SEQ ID NO: 53 or SEQ ID NO: 54 and conferring an increase in the amount of the fine chemical in an organism or a part thereof;
- (g) nucleic acid molecule encoding a polypeptide which is isolated with the aid of monoclonal and/or polyclonal antibodies against a polypeptide encoded by one of the nucleic acid molecules of (a) to (f) and conferring an increase in the amount of fine chemical in an organism or a part thereof;
- 10 (h) nucleic acid molecule encoding a polypeptide comprising the consensus sequence as depicted in SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 397, SEQ ID NO: 398, SEQ ID NO: 399 and/or SEQ ID NO: 400 and conferring an increase in the amount of the fine chemical in an organism or a part thereof; and
  - (i) nucleic acid molecule which is obtainable by screening a suitable nucleic acid library under stringent hybridization conditions with a probe comprising one of the sequences of the nucleic acid molecule of (a) to (k) or with a fragment thereof having at least 15 nt, preferably 20 nt, 30 nt, 50 nt, 100 nt, 200 nt or 500 nt of the nucleic acid molecule characterized in (a) to (k) and conferring an increase in the amount of the fine chemical in an organism or a part thereof,

whereby the nucleic acid molecule distinguishes over the sequence as depicted in SEQ ID NO: 1, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391or 393 by one or more nucleotides.

- A nucleic acid construct which confers the expression of the nucleic acid molecule of claim 6, comprising one or more regulatory elements.
  - 8. A vector comprising the nucleic acid molecule as claimed in claim 6 or the nucleic acid construct of claim 7.

- 9. The vector as claimed in claim 8, wherein the nucleic acid molecule is in operable linkage with regulatory sequences for the expression in a prokaryotic or eukaryotic, or in a prokaryotic and eukaryotic, host.
- 10. A host cell, which has been transformed stably or transiently with the vector as claimed in claim 8 or 9 or the nucleic acid molecule as claimed in claim 6 or the nucleic acid construct of claim 7 or produced as described in claim any one of claims 2 to 4.
  - 11. The host cell of claim 10, which is a transgenic host cell.
- The host cell of claim 10 or 11, which is a plant cell, an animal cell, a
   microorganism, or a yeast cell, a fungus cell, a prokaryotic cell, an eukaryotic cell or an archaebacterium.
  - 13. A process for producing a polypeptide, wherein the polypeptide is expressed in a host cell as claimed in any one of claims 9 to 11.
- 14. A polypeptide produced by the process as claimed in claim 13 or encoded by the nucleic acid molecule as claimed in claim 6 whereby the polypeptide 15 distinguishes over the sequence as depicted in SEQ ID NO: 2, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 20 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326, 328, 25 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392 or 394 by one or more amino acids.
  - 15. An antibody, which binds specifically to the polypeptide encoded by a nucleic acid sequence as claimed in claim 6 a).
- 30 16. A plant tissue, propagation material, harvested material or a plant comprising the host cell as claimed in claim 12, which is plant cell or an Agrobacterium.
  - 17. A method for screening for agonists and antagonists of the activity of a polypeptide encoded by the nucleic acid molecule of claim 6 conferring an increase in the amount of fine chemical in an organism or a part thereof comprising:

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- (a) contacting cells, tissues, plants or microorganisms which express the a polypeptide encoded by the nucleic acid molecule of claim 6 conferring an increase in the amount of the fine chemical in an organism or a part thereof with a candidate compound or a sample comprising a plurality of compounds under conditions which permit the expression the polypeptide;
- (b) assaying the fine chemical level or the polypeptide expression level in the cell, tissue, plant or microorganism or the media the cell, tissue, plant or microorganisms is cultured or maintained in; and
- (c) identifying a agonist or antagonist by comparing the measured fine chemical level or polypeptide expression level with a standard fine chemical or polypeptide expression level measured in the absence of said candidate compound or a sample comprising said plurality of compounds, whereby an increased level over the standard indicates that the compound or the sample comprising said plurality of compounds is an agonist and a decreased level over the standard indicates that the compound or the sample comprising said plurality of compounds is an antagonist.
  - 18. A process for the identification of a compound conferring increased fine chemical production in a plant or microorganism, comprising the steps:
    - (a) culturing a plant cell or tissue or microorganism or maintaining a plant expressing the polypeptide encoded by the nucleic acid molecule of claim 6 conferring an increase in the amount of the fine chemical in an organism or a part thereof and a readout system capable of interacting with the polypeptide under suitable conditions which permit the interaction of the polypeptide with dais readout system in the presence of a compound or a sample comprising a plurality of compounds and capable of providing a detectable signal in response to the binding of a compound to said polypeptide under conditions which permit the expression of said readout system and of the polypeptide encoded by the nucleic acid molecule of claim 6 conferring an increase in the amount of the fine chemical in an organism or a part thereof;
    - (b) identifying if the compound is an effective agonist by detecting the presence or absence or increase of a signal produced by said readout system.
  - 19. A method for the identification of a gene product conferring an increase in the fine chemical production in a cell, comprising the following steps:
- 35 (a) contacting the nucleic acid molecules of a sample, which can contain a candidate gene encoding a gene product conferring an increase in fine chemical after expression with the nucleic acid molecule of claim 6;

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- (b) identifying the nucleic acid molecules, which hybridize under relaxed stringent conditions with the nucleic acid molecule of claim 6;
- (c) introducing the candidate nucleic acid molecules in host cells appropriate for producing the fine chemical;
- 5 (d) expressing the identified nucleic acid molecules in the host cells;
  - (e) assaying the fine chemical level in the host cells; and
  - (f) identifying nucleic acid molecule and its gene product which expression confers an increase in the fine chemical level in the host cell in the host cell after expression compared to the wild type.
- 10 20. A method for the identification of a gene product conferring an increase in fine chemical production in a cell, comprising the following steps:
  - (a) identifying in a data bank nucleic acid molecules of an organism; which can contain a candidate gene encoding a gene product conferring an increase in the fine chemical amount or level in an organism or a part thereof after expression, and which are at least 30% homolog to the nucleic acid molecule of claim 6;
  - (b) introducing the candidate nucleic acid molecules in host cells appropriate for producing the fine chemical;
  - (c) expressing the identified nucleic acid molecules in the host cells;
  - (d) assaying the fine chemical level in the host cells; and
    - (e) identifying nucleic acid molecule and its gene product which expression confers an increase in the fine chemical level in the host cell after expression compared to the wild type.
- 21. A method for the production of an agricultural composition comprising the steps of the method of any one of claims 17 to 20 and formulating the compound identified in any one of claims 17 to 20 in a form acceptable for an application in agriculture.
- A composition comprising the nucleic acid molecule of claim 6, the polypeptide of claim 14, the nucleic acid construct of claim 7, the vector of any one of claims 8 or 9, an antagonist or agonist identified according to claim 17, the compound of claim 18, the gene product of claim 19 or 20, the antibody of claim 15, and optionally an agricultural acceptable carrier.

- 23. Use of the nucleic acid molecule as claimed in claim 6 for the identification of a nucleic acid molecule conferring an increase of the fine chemical after expression.
- 24. Use of the polypeptide of claim 14 or the nucleic acid construct claim 7 or the gene product identified according to the method of claim 18 or 19 for identifying compounds capable of conferring a modulation of the fine chemical levels in an organism.
- Food or feed composition comprising the nucleic acid molecule of claim 6, the polypeptide of claim 14, the nucleic acid construct of claim 7, the vector of claim 8 or 9, the antagonist or agonist identified according to claim 17, the antibody of claim 15, the plant or plant tissue of claim 16, the harvested material of claim 16, the host cell of claim 10 to 12 or the gene product identified according to the method of claim 19 or 20.
- Use of the nucleic acid molecule as claimed in claim 6 in mapping and breeding
   processes for the identification of plant varieties having and increased capacity
   for production of the fine chemical.

Figure 1: Protein alignment of Rho small GTPases from *Oryza sativa* cv. Noppon-Brarre (a japonica rice), *Brassica napus* cv. "AC Excel" "Quantum" and "Cresor" (canola), and *Glycine max* cv. Resuick (soybean). Boxes (doted line) represent the identical amino acid.

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aat Asn 145	aaa Lys	gct Ala	gat Asp	cta Leu	cat His 150	gaa Glu	aat Asn	cga Arg	cat His	gta Val 155	tct Ser	tct Ser	cag Gln	gaa Glu	gca Ala 160	480
caa Gln	gag Glu	tat Tyr	gca Ala	gag Glu 165	aag Lys	aat Asn	aat Asn	atg Met	gtt Val 170	ttc Phe	atc Ile	gag Glu	aca Thr	tca Ser 175	gca Ala	528
 aag Lys	aca Thr	gct Ala	gat Asp 180	Asn	ata	aac Asn	caa Gln	gta Val 185	ttt Phe	gag Glu	gaa Glu	att Ile	gcg Ala 190	aag Lys	agg Arg	576

180 600 ttg ccc agg cca acg gcg tct tga Leu Pro Arg Pro Thr Ala Ser

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Met Gly Cys Ser Ser Ser Val Pro Ala Arg Ser Thr Gly Gly Leu Asn

Asn Ile Ser Asn Asp Asn Ser Ala Thr Asp Ser Lys Asp Leu Arg Ala 20

Lys Leu Val Leu Leu Gly Asp Ser Gly Val Gly Lys Ser Cys Ile Val 40

Leu Arg Phe Val Arg Gly Gln Phe Asp Pro Thr Ser Lys Val Thr Val

Gly Ala Ser Phe Leu Ser Gln Thr Leu Ala Leu Glu Asp Ser Thr Ile

Val Lys Phe Glu Ile Trp Asp Thr Ala Gly Gln Glu Arg Tyr Ala Ala

Leu Ala Pro Leu Tyr Tyr Arg Gly Ala Ala Ala Val Val Val Tyr 100

Asp Ile Thr Ser Pro Glu Ser Phe Ser Lys Ala Gln Tyr Trp Val Lys 120 115

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Glu Leu Gln Lys His Gly Ser Pro Asp Ile Ile Met Val Leu Val Gly
130 140

Asn Lys Ala Asp Leu His Glu Asn Arg His Val Ser Ser Gln Glu Ala 145 150 155 160

Gln Glu Tyr Ala Glu Lys Asn Asn Met Val Phe Ile Glu Thr Ser Ala 165 170 175

Lys Thr Ala Asp Asn Ile Asn Gln Val Phe Glu Glu Ile Ala Lys Arg 180 185 190

Leu Pro Arg Pro Thr Ala Ser 195

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<212> DNA

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<220>

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			gat Asp												aac Asn		144
			gac Asp														192
65 65 65	cag Gln	gaa Glu	gat Asp	tac Tyr	aac Asn 70	aga Arg	ttg Leu	agg Arg	ccg Pro	cta Leu 75	agc Ser	tac Tyr	cgt Arg	ggc Gly	gcc Ala 80	- 4	240
gat	gtc	ttt	gtg	ctt	gcc	ttc	tcc	cta	gtg	agc	cga	gct	agc	tat	gag	2	288
qaA	Val	Phe	Val	Leu 85	Ala	Phe	Ser	Leu	Val 90	Ser	Arg	Ala	Ser	Tyr 95	Glu		•
			aag Lys												Gly ggg	. 3	336

6/291 100 105 110

			100													
gtg Val	cca Pro	att Ile 115	gtg Val	ttg Leu	gtt Val	gjå aaa	acc Thr 120	aaa Lys	ttg Leu	gat Asp	ctt Leu	cgt Arg 125	gaa Glu	gat Asp	aaa Lys	384
cac His	tac Tyr 130	tta Leu	ctt Leu	gac Asp	cat His	cct Pro 135	agc Ser	ttg Leu	gtg Val	cct Pro	gtg Val 140	act Thr	aca Thr	gca Ala	cag Gln	432
gga Gly 145	gag Glu	gaa Glu	ctc Leu	cgc Arg	aag Lys 150	cac His	att Ile	ggc Gly	gca Ala	acg Thr 155	tgt Cys	tac Tyr	atc Ile	gaa Glu	tgc Cys 160	480
agc Ser	tca Ser	aag Lys	aca Thr	cag Gln 165	cag Gln	aat Asn	gta Val	aaa Lys	gct Ala 170	gtg Val	ttt Phe	gat Asp	gct Ala	gcc Ala 175	atc Ile	528
aag Lys	gta Val	gta Val	atc Ile 180	aag Lys	cct Pro	cca Pro	aca Thr	aag Lys 185	cag Gln	agg Arg	gac Asp	agg Arg	aag Lys 190	aag Lys	aag Lys	576
aaa Lys	aca Thr	cgg Arg 195	cgc Arg	gga Gly	tgt Cys	tct Ser	ttc Phe 200	ttc Phe	tgc Cys	aag Lys	ggt Gly	gtc Val 205	atg Met	tcc Ser	aga 'Arg	624
aga	agg	cta	gta	tgc	ttc	aag	tga									648
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<213> Oryza sativa

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Val Val Val Asp Gly Thr Thr Val Asn Leu Gly Leu Trp Asp Thr Ala 50 55 60

Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala 65 70 75 80

Asp Val Phe Val Leu Ala Phe Ser Leu Val Ser Arg Ala Ser Tyr Glu 85 90 95

				•						-							•	•
	Asn	Val	Met	Lys 100	Lys	Trp	Leu	Pro	Glu 105	Leu	Gln	His	Tyr	Ala 110	Pro	Gly		٠.
	Val	Pro	Ile 115	Val	Leu	Val	Gly	Thr 120	Lys	Leu	Asp	Leu	Arg 125	Glu	Asp	Lys		
	His	Tyr 130	Leu	Leu	Asp	His	Pro 135	Ser	Leu	Val	Pro	Val 140		Thr	Ala	Gln	·	٠.
	Gly 145	Glu	Glu	Leu	Arg	Lys 150	His	Ile	Gly	Ala	Thr 155	Cys	Tyr	Ile	Glu	Cys 160		
	Ser	Ser	Lys		Gln 165	Gln	Asn	Val	Lys	Ala 170	Val	Phe	Asp	Ala	Ala 175	Ile	•	
٠	Lys	Val	Val	Ile 180	Lys	Pro	Pro	Thr	Lys 185	Gln	Arg	Asp	Arg	Lys 190	Lys	Lys		
	Lys	Thr	Arg 195	Arg	Gly	Cys	Ser	Phe 200	Phe	Cys	Lys	Gly	Val 205	Met	Ser	Arg		
	Arg	Arg 210	Leu	Val	Сув	Phe	Lys 215											
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	<213	3> 1	Brass	sica	napı	ıs												•
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	<220	١.																
					٠.											•		
	<223	L> (	CDS			•								.:			•	
	<222	2>	(1).	. (591	L)												•	٠
	<223	3>									•			•				
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												agc Ser					· .	96
												agt Ser				gtt Val		144
												gat Asp						192

60 55 50 gaa gac tat aac agg tta aga cca ttg agt tac cgt ggt gca gat gtc 240 Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 70 tto att ott got tto tot ott att ago aaa got ago tac gag aac ata 288 Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Ile gcc aag aag tgg att cct gag ctc agg cat tat gcc cct gga gtt cct 336 Ala Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro 100 atc att ctc gtg ggg aca aaa ctc gat ctt cga gat gac aag cag ttc 384 Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe 120 115 ttc ata gac cat ccc ggt gca gtg cca atc act aca aac cag gga gag 432 Phe Ile Asp His Pro Gly Ala Val Pro Ile Thr Thr Asn Gln Gly Glu 135 gaa cta aag aaa ctc ata gga tct cca gtt tac att gaa tgt agt tca 480 Glu Leu Lys Lys Leu Ile Gly Ser Pro Val Tyr Ile Glu Cys Ser Ser aag acg cag cag aat gtc aaa gca gtc ttt gac gca gct att aaa gtg 528 Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val 165 gtg ctt cag cca cca aaa tca aag aag aag aaa aag aac aag aat cgt 576 Val Leu Gln Pro Pro Lys Ser Lys Lys Lys Lys Asn Lys Asn Arg 185 180 591 tgc gtt ttc ttg tga Cys Val Phe Leu 195 <210> <211> 196 <212> PRT <213> Brassica napus <400> Met Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val Val Asp Gly Asn Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln 50 Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val

9/291 70 75 65 Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Ile Ala Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro 105 Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe 120 Phe Ile Asp His Pro Gly Ala Val Pro Ile Thr Thr Asn Gln Gly Glu 135 130 140 Glu Leu Lys Lys Leu Ile Gly Ser Pro Val Tyr Ile Glu Cys Ser Ser Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val Val Leu Gln Pro Pro Lys Ser Lys Lys Lys Lys Asn Lys Asn Arg 185 Cys Val Phe Leu 195 <210> 9 <211> .597 <212> DNA <213> Brassica napus <220> <221> CDS <222> (1)..(597) <223> atg agt gct tcg agg ttt atc aag tgt gtc acc gtc ggc gac ggc gct Met Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala 48 gtc gga aag act tgt ctg ctc atc tcc tac act agc aac act ttc ccc 96

Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro

acg gac tat gtg cca act gtg ttt gat aat ttc agc gcg aat gtg att Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Ile

25

20

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gtg Val	gat Asp 50	Gly 333	aac Asn	act Thr	Ile	aac Asn 55	ttg Leu	gga Gly	ttg Leu	tgg Trp	gat Asp 60	act Thr	gca Ala	gly ggg	caa Gln		192
gag Glu 65	gac Asp	tac Tyr	aat Asn	Arg	cta Leu .70	aga Arg	cca Pro	ttg Leu	agc Ser	tat Tyr 75	cgc Arg	ggc	gca Ala	gat Asp	gtc Val 80		240
ttc Phe	tta Leu	ctc Leu	gct Ala	ttc Phe 85	tcc Ser	ctt Leu	gtc Val	agc Ser	aaa Lys 90	gct Ala	agc Ser	tat Tyr	gaa Glu	aat Asn 95	gtt Val		288
tct Ser	aaa Lys	aag Lys	tgg Trp 100	gta Val	cct Pro	gaa Glu	ctg Leu	aga Arg 105	cat His	tat Tyr	gct Ala	cct Pro	ggt Gly 110	gtt Val	cca Pro		336
atc Ile	atc Ile	ctc Leu 115	gtc Val	gga Gly	acc Thr	aag Lys	ctt Leu 120	gat Asp	ctt Leu	cga Arg	gat Asp	gac Asp 125	aag Lys	caa Gln	ttc Phe		384
ttt Phe	gtt Val 130	gag Glu	cac His	cct Pro	ggt Gly	gct Ala 135	Val	cct Pro	atc Ile	tct Ser	act Thr 140	gct Ala	cag Gln	ggt Gly	gaa Glu		432
gaa Glu 145	Leu	aag Lys	aag Lys	gtg Val	att Ile 150	GIY	gca Ala	cct Pro	gct Ala	tat Tyr 155		gaa Glu	tgo Cys	agt Ser	gca Ala 160	·	480
aaa Lys	aca Thr	caa Glr	cag Glr	aat Asn 165	vaı	aaa Lys	gcg Ala	gtg Val	ttt Phe	يرجم .	gcg Ala	g gct a Ala	ato Ile	aag Lys 175	gta Val		528
gtt Va]	cto Lev	caa Glr	cca Pro 180	Pro	aaa Lys	aac Asr	aag Lys	aag Lys 185	Arg	l gag	g aag E Lyg	g aga s Arg	a aag Lys 190		cag Gln		576
aaa Lys	a gct s Alá	tgi Cyi	t tct s Sei	ata r Ile	a ttg e Lei	g tga	a										597
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<2	12>	PRT															
<2	13>	Bra	ssic	a na	pus												
<b>~</b> 4	00>	10															

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Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro 20

Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Ile

Val Asp Gly Asn Thr Ile Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln 50 55 60

Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 65 70 75 80

Phe Leu Leu Ala Phe Ser Leu Val Ser Lys Ala Ser Tyr Glu Asn Val 85 90 95

Ser Lys Lys Trp Val Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro
100 105 110

Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe 115 120 125

Phe Val Glu His Pro Gly Ala Val Pro Ile Ser Thr Ala Gln Gly Glu 130 135 140

Glu Leu Lys Lys Val Ile Gly Ala Pro Ala Tyr Ile Glu Cys Ser Ala 145 150 155 160

Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val 165 170 175

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<222> (1)..(591)

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48

96

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acg Thr	gat Asp	tat Tyr 35	gtt Val	cca Pro	aca Thr	gtg Val	ttt Phe 40	gac Asp	aat Asn	ttc Phe	agt Ser	gct Ala 45	aat Asn	gta Val	acg Thr	144
gtg Val	gat Asp 50	ggt Gly	agt Ser	act Thr	gtt Val	aat Asn 55	ctt Leu	ggt Gly	tta Leu	tgg Trp	gac Asp 60	act Thr	gca Ala	gga Gly	caa Gln	192
gaa Glu 65	gat Asp	tac Tyr	aac Asn	agg Arg	cta Leu 70	agg Arg	cct Pro	tta Leu	agc Ser	tat Tyr 75	aga Arg	gga Gly	gct Ala	gat Asp	gtg Val 80	240
ttt Phe	ttg Leu	ttg Leu	tgc Cys	tat Tyr 85	tct Ser	ctç Leu	atc Ile	agc Ser	aaa Lys 90	gcc Ala	agt Ser	tat Tyr	gag Glu	aac Asn 95	atc Ile	288
Ser	Lys	. Lys	tgg Trp 100	Ile	Pro	GIU	ьeu	105	птэ	171	7110		110			336
Ile	val	115		Gly	Thr	гÀз	120	Asp	neu	. Arg	FIDE	125				384
Leu	130	Asp	) His	Pro	о Сту	135	Ala	LAIG	116		140	)		_	gaa Glu	432
gaa Glu 14!	ı Leı	aag Lys	g aaa s Lys	ato Met	att : Ile 150	GT)	gca Ala	gto Val	act Thr	tat Tyr 155		gag Glu	g tgo 1 Cys	ago Ser	tcc Ser 160	480
aaa Ly:	a aca s Thi	a cag	g cto n Lei	g aat 1 Ast 16!	ı va.	g aag L Lys	g aca	a gtt r Val	ttt L Phe 170	L	ge Ala	t gca a Ala	a ata a Ile	a aag E Lys 175	g gtt s Val	528
gc Al	a tt a Le	g aa u Ly	g cc s Pr 18	o Pr	a aag o Ly	g cca s Pro	a aa o Ly	g aag s Lys 18	s шy	a cca s Pro	a cg o Ar	c aa g Ly	g aaa s Lya 19	a agg s Arg	g acc g Thr	576
tg Cy	t ac s Th	t tt r Ph 19	c ct e Le 5	c tg u	a									•		591
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Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro

Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Thr

48

Val Asp Gly Ser Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln 50 55 60

Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 65 70 75 80

Phe Leu Leu Cys Tyr Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Ile 85 90 95

Ser Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Ala Pro Asn Val Pro 100 105 110

Ile Val Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe 115 120 125

Leu Ile Asp His Pro Gly Ser Ala Arg Ile Thr Thr Ala Gln Gly Glu 130 135 140

Glu Leu Lys Lys Met Ile Gly Ala Val Thr Tyr Ile Glu Cys Ser Ser 145 150 155 160

Lys Thr Gln Leu Asn Val Lys Thr Val Phe Asp Ala Ala Ile Lys Val 165 170 175

Ala Leu Lys Pro Pro Lys Pro Lys Lys Lys Pro Arg Lys Lys Arg Thr 180 185 190

Cys Thr Phe Leu 195

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<212> DNA

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<222> (1)..(594)

<223>

gtg gga aag act tgc atg ctt atc tct tac act agc aac act ttc ccc

•	O 200	5/014	828												101	/ 121 200	, ,, , , , ,	
									14/29							_		
	Val	Gly	Lys	Thr 20	Cys	Met :	Leu	Ile	Ser 25	Tyr	Thr	Ser	Asn	Thr 30	Phe	Pro		
	acg Thr	gat Asp	tat Tyr 35	gtt Val	cct Pro	aca Thr	Val	ttc Phe 40	gac Asp	aat Asn	ttc Phe	agt Ser	gca Ala 45	aat Asn	gtt Val	gtg Val		144
	gtt Val	gat Asp 50	ggc Gly	agc Ser	aca Thr	gtt Val	aac Asn 55	ctg Leu	gga Gly	ttg Leu	tgg Trp	gac Asp 60	act Thr	gct Ala	gga Gly	cag Gln		192
	gaa Glu 65	gat Asp	tac Tyr	aac Asn	agg Arg	ctt Leu 70	agg Arg	cca Pro	ttg Leu	agt Ser	tac Tyr 75	aga Arg	gga Gly	gca Ala	gat Asp	gtg Val 80		240
	ttc Phe	ttg Leu	ctg Leu	gcc Ala	ttt Phe 85	tcc Ser	ctc Leu	atc Ile	agc Ser	aaa Lys 90	gcc Ala	agc Ser	tat Tyr	gaa Glu	aat Asn 95	ata Ile		288
	tct Ser	aaa Lys	aag Lys	tgg Trp 100	att Ile	cct Pro	gaa Glu	ttg Leu	aga Arg 105	cat His	tat Tyr	gcc Ala	cca Pro	act Thr 110	٧٨٢	cct Pro		336
	att Ile	gta Val	ctg Leu 115	. Val	gga Gly	act Thr	aaa Lys	ctt Leu 120	Asp	ttg Leu	agg Arg	gaa Glu	gac Asp 125	_ A9	caa Gln	tat Tyr		384
	Leu	130	Asp	His	Pro	GIY	135	Thi	Ala	TIE	MIG	140	)	. 011	,	gaa Glu		432
	Glu 145	Leu ;	Lys	. Lys	: Ala	150	GTÅ	Ala	i Ala	. vai	155	5	. 010	. 0,-		tca Ser 160		480
	aag Lys	act Thr	cag Glr	g cag n Glr	g aat n Asr 165	ı vaı	r aag . Lys	gco Ala	gtg a Val	ttt Phe 170	ر حمد د	get Ala	gca a Ala	a ato	aaq E Lys 17!	g gtt s Val		528
	gtt Val	ttg L Lei	g caa 1 Gl	a cca n Pro 180	o Pro	aag b Lys	tco Ser	aaq Ly	g aaa s Lys 189	з та	a gga s Gly	a aaq y Ly	g aag s Ly	g aag s Ly: 19		c acg n Thr		576
	pro	t tgt o Cys	gt s Va 19	l · Pho	c cto e Le	c tga u	a											594
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Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro 20 25 30

Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val
35 40 45

Val Asp Gly Ser Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln 50 55 60

Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 65 70 75 80

Phe Leu Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Ile 85 90 95

Ser Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Ala Pro Thr Val Pro 100 105 110

Ile Val Leu Val Gly Thr Lys Leu Asp Leu Arg Glu Asp Arg Gln Tyr
115 120 125

Leu Ile Asp His Pro Gly Thr Thr Ala Ile Ala Thr Ala Gln Gly Glu 130 135 140

Glu Leu Lys Lys Ala Ile Gly Ala Ala Val Tyr Ile Glu Cys Ser Ser 145 150 155 160

Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val 165 170 175

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<222> (1)..(591)

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acg Thr	gac Asp	tat Tyr 35	Val	ccc Pro	acc Thr	gtt Val	ttt Phe 40	gac Asp	aat Asn	ttc Phe	agt Ser	gct Ala 45	aat Asn	gtg Val	gtg Val		144
gtg Val	gat Asp 50	gga Gly	agc Ser	acc Thr	gta Val	aac Asn 55	cta Leu	gga Gly	ttg Leu	tgg Trp	gat Asp 60	aca Thr	gct Ala	ggt Gly	cag Gln		192
gag Glu 65	gat Asp	tac Tyr	aat Asn	aga Arg	tta Leu 70	aga Arg	ccc Pro	ttg Leu	agc Ser	tat Tyr 75	cga Arg	gga Gly	gct Ala	gat Asp	gtc Val 80		240
ttc Phe	ata Ile	ctt Leu	gcc Ala	ttt Phe 85	tct Ser	ctc Leu	ata Ile	agc Ser	aag Lys 90	gct Ala	agc	tat Tyr	gaa Glu	aat Asn 95	att Ile		288
gca Ala	aag Lys	aag Lys	tgg Trp	Ile	cct Pro	gaa Glu	cta Leu	agg Arg 105	111.5	tat Tyr	gcc	ect Pro	ggt Gly 110	gtt Val	cca Pro		336
Ile	e Ile	Lev 115	ı Val	. Сту	Thr	гу	120	)	, 100		,	125	5		ttt Phe		384
Phe	e Met 130	Ası	His	e Pro	GTĀ	135	i va.	L PIC	, 110		14	0		•	a gaa y Glu	٠.	432
G1 <sup>.</sup> 14	u Lei 5	u Arg	a rà	в тел	150	)	, 41			15	5		_		t tcc r Ser 160		480
Ŀу	s Th	r Gl:	n Gl	n Asi	n va. 5	г гу	S AL	a va	17	0	P			17			528
gt Va	t at 1 Il	c ca e Gl	a cc n Pr 18	o Pr	a aag o Lys	g ct	a aa u Ly	g aa s Ly 18	S TI	g ag s Ar	a aa g Ly	a ac	a ca ir Gl 19	g aa n Ly 00	a gct s Ala		576
.tg	jc to /s Se	c ater Il	e Le	a tg	a.												591
<2	210>	16															
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<:	212>	PR	r														
<	213>	G1;	ycin	e mai	ĸ												
	400>																
М	et S	er A	la S	er A	rg Pl	ne I	le I	ys C	ys V	al T	hr V	al G	ly A	sp G	ly Ala	a	

Met Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala 1 5 10

Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro 20 25 30

Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val
35 40 45

Val Asp Gly Ser Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln 50 55 60

Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 65 70 75 80

Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Ile 85 90 95

Ala Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro
100 105 110

Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe
115 120 125

Phe Met Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly Glu 130 135 140

Glu Leu Arg Lys Leu Ile Gly Ala Pro Ala Tyr Ile Glu Cys Ser Ser 145 150 155 160

Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val 165 170 175

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Cys Ser Ile Leu 195

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## 18/291 Met Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala gtg ggc aaa acc tgt ttg ctt att tcc tac acc agc aac act ttt ccc 96 Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro acc gat tat gtg ccg act gtt ttt gac aat ttc agc gca aat gtg gtt 144 Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val gtc aat ggg agc att gtg aat ctg ggt ttg tgg gat act gct gga caa 192 Val Asn Gly Ser Ile Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln gag gat tat aac aga tta aga cct ttg agt tac cgt ggt gcc gat gtt 240 Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 70 ttc ata ctg gct ttc tct ctc ata agc aag gcc agt tat gaa aat gtc 288 Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val tet aaa aag tgg att eeg gag ttg aag cat tat get eet ggt gte eee 336 Ser Lys Lys Trp Ile Pro Glu Leu Lys His Tyr Ala Pro Gly Val Pro att att ctg gtt ggc aca aag ctt gac ctt cgg gat gat aag cag ttc 384 Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe tgc att gac cat cet ggt gcc gta cet att acc aca get cag gga gaa 432 Cys Ile Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly Glu 135 gag ctt agg aag ctg att aat gcg cca gct tac att gaa tgc agt tca 480 Glu Leu Arg Lys Leu Ile Asn Ala Pro Ala Tyr Ile Glu Cys Ser Ser 155 150 aaa aca cag gag aac gtg aag gca gtc ttt gat gca gcc ata aga gtt 528 Lys Thr Gln Glu Asn Val Lys Ala Val Phe Asp Ala Ala Ile Arg Val 170 165 gtc ctt caa cca cct aag cag aag aaa aag aag ggt aaa gca caa aag Val Leu Gln Pro Pro Lys Gln Lys Lys Lys Gly Lys Ala Gln Lys 576 594 gcc tgt tcg ata ttg tga Ala Cys Ser Ile Leu <210> 18 197 <211> <212> PRT

<400> 18

<213> Glycine max

Met Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala 1 5 10 15 Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro 20 25 30

Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val 35 40 45

Val Asn Gly Ser Ile Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln 50 55

Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 65 70 75 80

Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val

Ser Lys Lys Trp Ile Pro Glu Leu Lys His Tyr Ala Pro Gly Val Pro 100 105 110

Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe 115 120 125

Cys Ile Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly Glu 130 135 140

Glu Leu Arg Lys Leu Ile Asn Ala Pro Ala Tyr Ile Glu Cys Ser Ser 145 150 155 160

Lys Thr Gln Glu Asn Val Lys Ala Val Phe Asp Ala Ala Ile Arg Val 165 170 175

Val Leu Gln Pro Pro Lys Gln Lys Lys Lys Gly Lys Ala Gln Lys 180 185 190

Ala Cys Ser Ile Leu 195

<210> 19

<211> 594

<212> DNA

<213> Glycine max

<220>

<221> CDS

<222> (1)..(594)

<223>

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gtt Val	ggc Gly	aag Lys	act Thr 20	tgc Cys	atg Met	ctc Leu	atc Ile	tcc Ser 25	tac Tyr	acc Thr	agc Ser	aac Asn	act Thr 30	ttt Phe	ect Pro	96
acg Thr	gac Asp	tac Tyr 35	gtg Val	cca Pro	act Thr	gtc Val	ttt Phe 40	gac Asp	aat Asn	ttc Phe	agt Ser	gca Ala 45	aat Asn	gtc Val	gtt Val	144
gtg Val	gat Asp 50	gga Gly	agc Ser	act Thr	gtg Val	aat Asn 55	ctt Leu	Gly	ttg Leu	tgg Trp	gat Asp 60	act Thr	gct Ala	ggc	caa Gln	192
gaa Glu 65	gat Asp	tac Tyr	aat Asn	aga Arg	ttg Leu 70	aga Arg	ccc Pro	tta Leu	agc Ser	tat Tyr 75	cgt Arg	gga	gca Ala	gat Asp	gta Val 80	240
ttc Phe	ctg Leu	ctt Leu	gct Ala	ttc Phe 85	tct Ser	ctc Leu	ata Ile	agc Ser	agg Arg 90	gcc	ago Ser	tat Tyr	gaa Glu	aat Asn 95	gtt Val	288
gcc Ala	aag Lys	aaa Lys	tgg Trp	Ile	cct Pro	gag Glu	ttg Lev	agg Arg 105	HIS	tat Tyr	gct Ala	cct Pro	ggt Gl <sub>y</sub> 110		cca Pro	336
att	att Ile	cti Lei 11!	ı Va.	c gga	aca Thr	aaa Lys	ctt Lev	r war	ctt Lev	cgg Arg	g gat g Asp	gat Ası 12	3	g cag s Glr	ttc n Phe	384
ttt Phe	caa Gli	n Asj	c ca p Hi	t cct s Pro	ggt Gly	gca Ala	ı va.	g cct L Pro	ato	aco Thi	c aca c Thi		a cag a Gli	g ggt	t gag y Glu	432
gaa Glu 145	1 Le	g ag u Ar	a aa g Ly	g cti s Le	t ato u Ile 150	S GT	gci y Ala	t cca	a att	t tag e Ty: 15		t ga e Gl	a tg u Cy	t ag s Se	t tca r Ser 160	480
aaa Lys	a ac s Th	a ca r Gl	a ca n Gl	g aa n As 16	n va	g aag l Ly	g gc	t gt a Va	t tt 1 Ph 17		t gc p Al	a gc a Al	c at a Il	c aa e Ly 17	g gta s Val 5	528
gti Va	t ct l Le	c ca u Gl	g co n Pr 18	o Pr	a aa o Ly	g ca s Gl	g aa n Lŷ	g aa s Ly 18	o by	g aa s Ly	g ag s Ar	a aa g Ly	g gg rs Gl 19	-	a aag n Lys	576
gc Al	c tg a Cy	rs Se	ec at er II 95	t tt Le Le	g tg	a										594

<210> 20

<211> 197

<212> PRT

<213> Glycine max

<400> 20

Met Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala 1 5 10 15

Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro 20 25 30

Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val 35 40 45

Val Asp Gly Ser Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln 50 55

Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 70 75 80

Phe Leu Leu Ala Phe Ser Leu Ile Ser Arg Ala Ser Tyr Glu Asn Val 85 90 95

Ala Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro 100 105 110

Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe 115 120 125

Phe Gln Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly Glu 130 135 140

Glu Leu Arg Lys Leu Ile Gly Ala Pro Ile Tyr Ile Glu Cys Ser Ser 145 150 155 160

Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val 165 170 175

Val Leu Gln Pro Pro Lys Gln Lys Lys Lys Lys Arg Lys Gly Gln Lys 180 185 190

Ala Cys Ser Ile Leu

<210> 21

<211> 594

<212> DNA

<213> Glycine max

<220>

<221> CDS

<222> (1)..(594)

<223>

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gtt Val	ggc Gly	aag Lys	act Thr 20	Çya tgc	atg Met	ctc Leu	atc Ile	tcc Ser 25	tac Tyr	acc Thr	agc Ser	aac Asn	act Thr 30	ttt Phe	Pro	96
acg Thr	gac Asp	tac Tyr 35	gtg Val	cca Pro	act Thr	gtc Val	ttt Phe 40	gac Asp	aat Asn	ttc Phe	agt Ser	gca Ala 45	aat Asn	gtc Val	gtt Val	144
gtg Val	gat Asp 50	gga Gly	agc Ser	act Thr	gtg Val	aat Asn 55	ctt Leu	GJA 333	ttg Leu	tgg Trp	gat Asp 60	act Thr	gct Ala	ggc	caa Gln	192
gaa Glu 65	gat Asp	tac Tyr	aat Asn	aga Arg	ttg Leu 70	aga Arg	ccc Pro	tta Leu	agc Ser	tat Tyr 75	cgt Arg	gga Gly	gca Ala	gat Asp	gta Val 80	240
ttc Phe	ctg Leu	ctt Leu	gct Ala	ttc Phe 85	tct Ser	ctc Leu	ata Ile	agc Ser	agg Arg 90	gcc Ala	agc Ser	tat Tyr	gaa Glu	aat Asn 95	gtt Val	288
gcc Ala	aag Lys	aaa Lys	tgg Trp 100	ITE	cct	gag Glu	ttg Leu	agg Arg 105	пто	tat Tyr	gct Ala	cct Pro	ggt Gly 110		cca Pro	336
att Ile	att Ile	ctt Leu 115	Val	gga Gly	aca Thr	aaa Lys	ctt Leu 120	. Asp	ctt Leu	cgg Arg	gat	gat Asp 125	плэ	cag Gln	ttc Phe	384
ttt Phe	caa Gln 130	Asp	cat His	cct Pro	ggt Gly	gca Ala 135	Val	ect Pro	ato Ile	acc Thr	aca Thr	. ATG	cag Glm	ggt Gly	gag Glu	432
gaa Glu 145	Let	aga Arg	aag Julys	g ctt s Lev	atc Ile 150	GIA	gct Ala	cca Pro	att Ile	tac Tyr 155		gaa Glu	tgt Cys	agt Ser	tca Ser 160	480
aaa Lys	aca Thi	a caa c Gli	a cag n Gli	g aat n Asi 165	ı Val	aag Lys	gct Ala	gtt Val	ttt L Phe 170	: AS	gca Ala	a gco a Ala	ato a Ile	aag Lys 17	g gta s Val	528
gtt Val	cto Le	c caq ı Glı	g cc 1 Pro 18	o Pro	a aag o Lys	g cag	aaq Ly	g aaa 5 Lys 18!	з та	g aaq s Lys	g aga	a aaq g Ly:	9 998 8 Gly 190	,	a aag n Lys	576
gcc Ala	tg Cy	t tc s Se 19	r Il	t tt e Le	g tga u											594

<210> 22

<211> 197

<212> PRT

<213> Glycine max

<400> 22

WO 2005/014828 PCT/EP2004/008136

Met Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala

1 5 10 15

Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro 20 25 30

Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val 35 40 45

Val Asp Gly Ser Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln 50 55 60

Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 65 70 75 80

Phe Leu Leu Ala Phe Ser Leu Ile Ser Arg Ala Ser Tyr Glu Asn Val 85 90 95

Ala Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro 100 105 110

Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe 115 120 125

Phe Gln Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly Glu 130 135 140

Glu Leu Arg Lys Leu Ile Gly Ala Pro Ile Tyr Ile Glu Cys Ser Ser 145 150 155 160

Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val 165 170 175

Val Leu Gln Pro Pro Lys Gln Lys Lys Lys Lys Arg Lys Gly Gln Lys 180 185 190

Ala Cys Ser Ile Leu 195

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<220>

<221> CDS

<222> (1)..(639)

<223>

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gat Asp	gga Gly	gct Ala	gta Val 20	gly aaa	aag Lys	acc Thr	tgc Cys	atg Met 25	ctc Leu	att Ile	tgc Cys	tat Tyr	acc Thr 30	agc Ser	aac Asn	96
Lys	Phe	Pro 35	Thr	Asp	TYT	TTE	40	act Thr	val	rnc	- Lug	45				144
Asn	Val 50	Val	Val	Glu	GTÀ	55	THE	val	ASII	пец	60	202				
Ala 65	Gly	Gln	Glu	Asp	79°	ASI	Arg		ALG	75	шси		-1-	3	80	240
Ala	Asp	Val	Phe	Val 85	Leu	Ala	Pne	. Ser	90	Val	DCI			95	tat Tyr	288
Glu	Asn ·	. Val	100	Lys )	г гла	TIL	TIE	105		. LCG			110	)	cct Pro	336
ggg	ato	ccg Pro 115	Let	g gtg 1 Val	g tta L Lei	gtt Val	ggc L Gly 120	1111	aaa Lys	ttg Lev	gat L Asp	Lev 125		ı gaa g Gli	a gac ı Asp	384
aag Lys	cac His	з Туз	atg Met	g gct : Ala	gat a Ası	cat Hi:	S PIG	ago Sei	tto Lei	g gtg 1 Val	J CC L Pro 140		g act L Thi	act Th	t gat r Asp	432
caa Gl: 14	a Gl	t gag	g gaa u Gli	a cto u Le	c cg <sup>1</sup> u Ar	агх	a ca s Hi	c att	gga e Gl	a gct y Ala 15		c tac r Ty:	c tai	t at r Il	t gag e Glu 160	480
tg Cy	c ag s Se	c tc r Se	a aa r Ly	a ac s Th 16	r GI	g ca n Gl	g aa n As	t gte n Va	g aag l Ly: 17		a gt a Va	t tt	t ga e As	4	t gct a Ala 5	528
at Il	t ag e Ar	a at g Me	g gt t Va 18	1 II	c aa e Ly	g co s Pr	t cc o Pr	a ca o Gl 18	и гъ	g ca s Gl	a aa n As	.c ga n Gl	g aa u Ly 19		a aag g Lys	576
aa Ly	a aa s Ly	a co s Pr 19	O Ar	rt gg g Gl	rc to .y Cy	rt tt rs Pl	c ct ne Le 20	u As	c gt n Va	c ct l Le	c tg u Cy	rt cg rs Ar 20	J	g aa g As	ac att sn Ile	624
		g Le	t aa eu Ly		ja				•							639

<210> 24

<211> 212

<212> PRT

<213> Glycine max

<400> 24

Met Ala Ser Ala Thr Ala Pro Arg Phe Ile Lys Cys Val Thr Val Gly
1 5 10 15

Asp Gly Ala Val Gly Lys Thr Cys Met Leu Ile Cys Tyr Thr Ser Asn 20 25 30

Lys Phe Pro Thr Asp Tyr Ile Pro Thr Val Phe Asp Asn Phe Ser Ala 35 40 45

Asn Val Val Val Glu Gly Ile Thr Val Asn Leu Gly Leu Trp Asp Thr 50 55 60

Ala Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly 65 70 75 80

Ala Asp Val Phe Val Leu Ala Phe Ser Leu Val Ser Arg Ala Ser Tyr 85 90 95

Glu Asn Val Leu Lys Lys Trp Ile Pro Glu Leu Gln His Phe Ala Pro 100 105 110

Gly Ile Pro Leu Val Leu Val Gly Thr Lys Leu Asp Leu Arg Glu Asp 115 120 125

Lys His Tyr Met Ala Asp His Pro Ser Leu Val Pro Val Thr Thr Asp 130 140

Gln Gly Glu Glu Leu Arg Lys His Ile Gly Ala Thr Tyr Tyr Ile Glu 145 150 155 160

Cys Ser Ser Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala 165 170 175

Ile Arg Met Val Ile Lys Pro Pro Gln Lys Gln Asn Glu Lys Arg Lys 180 185 190

Lys Lys Pro Arg Gly Cys Phe Leu Asn Val Leu Cys Arg Arg Asn Ile 195 200 205

Val Arg Leu Lys 210

<210> 25

<211> 762

<212> DNA

<213> Brassica napus

<220>

<221> CDS

<222> (1)..(762)

<223>

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gtt Val	caa Gln	tac Tyr	agc Ser 20	ttc Phe	agc Ser	gat Asp	ggt Gly	gga Gly 25	tgg Trp	gga Gly	gcc Ala	act Thr	ctc Leu 30	gct Ala	aac Asn		96 ·
atc Ile	tac Tyr	tct Ser 35	cgc Arg	acg Thr	gct Ala	gac Asp	gta Val 40	atc Ile	ctt Leu	cgt Arg	gly aaa	tat Tyr 45	gct Ala	ggt Gly	tgg Trp		144
aac Asn	tcc Ser 50	aga Arg	tct Ser	gcc Ala	ttg Leu	aag Lys 55	gtg Val	tta Leu	aac Asn	caa Gln	gtg Val 60	ttc Phe	cca Pro	aag Lys	gat Asp		192
gct Ala 65	gtt Val	ata Ile	caa Gln	cct Pro	tct Ser 70	ttg Leu	gtg Val	ata Ile	gtc Val	tat Tyr 75	ttc Phe	gga Gly	GJÅ 333	aat Asn	gat Asp 80		240
tca Ser	atg Met	cct Pro	cct Pro	cat His 85	cca Pro	tca Ser	gly aaa	caa Gln	gga Gly 90	cct Pro	cat His	gtt Val	cct Pro	ctc Leu 95	tct Ser		288
gaa Glu	ttc Phe	act Thr	gag Glu 100	aac Asn	atg Met	agg Arg	aag Lys	atc Ile 105	gga Gly	gag Glu	cat His	ctt Leu	ttg Leu 110	agc Ser	ctc Leu		336
tcg Ser	gac Asp	aag Lys 115	Thr	cgt Arg	gtc Val	att Ile	ttt Phe 120	Leu	act Thr	ccc Pro	cca Pro	cca Pro 125	Met	aac Asn	gag Glu		384
aga · Arg	caa Gln 130	Ile	caa Gln	cta Leu	gtg Val	ttt Phe 135	Gly	gat Asp	gca Ala	atg Met	aga Arg 140	GTA	Arg	agt Ser	aac Asn		432
gag Glu 145	Leu	tgt Cys	cgt Arg	cca Pro	tac Tyr 150	Ala	gaa Glu	gcg Ala	ttg Leu	ttg Leu 155	ASI	cta Leu	tgo Cys	aga Arg	gag Glu 160		480
ato Ile	aat Asn	gtg Val	aaa Lys	ggt Gly 165	/ Ile	gat Asp	ctt Lev	tgg Trp	aac Asr 170	Ala	ata Ile	. cag Glr	g Caa	caa Gln 175	gat Asp		528
gat Asp	tgg Trp	r tta Lev	cac His	Thi	tgo Cys	tto Phe	act Thi	gac Asp 185	Gl	ato Ile	cat His	tto Phe	ace Thr	Ala	aag Lys		576
gcg	g ago a Sei	gag Glu 195	ıIle	gtg Val	g gtg l Val	g aag L Lys	g gag Gli 200	ı IIe	ttg Lei	g aaa 1 Lys	gta Val	gto Val 209	LAT	a gaa g Glu	a gct 1 Ala		624
ga	t tgg	g aaa	a cc	g ag	t ctt	gaq	c ag	gaag	g tca	a tta	CCC	g gti	t gag	g ttt	cca		672

	7	/ <b>?</b> 0	1
Z	"	29	1

Asp Trp Lys Pro Ser Leu Asp Arg Lys Ser Leu Pro Val Glu Phe Pro 210 215 220

ttt gat tct ggt cta cca aac tcc cca aga cat agt gat cta gaa tta 720
Phe Asp Ser Gly Leu Pro Asn Ser Pro Arg His Ser Asp Leu Glu Leu
225 230 235 240

act aga aac aag aag ttg gag cct cgt atg gcc cga ttg taa 762
Thr Arg Asn Lys Leu Glu Pro Arg Met Ala Arg Leu
245 250

<210> 26

<211> 253

<212> PRT

<213> Brassica napus

<400> 26

Met Val Gly Pro Gly Arg Pro Gln Ile Val Leu Phe Gly Ser Ser Ile 1 10 15

Val Gln Tyr Ser Phe Ser Asp Gly Gly Trp Gly Ala Thr Leu Ala Asn 20 25 30

Ile Tyr Ser Arg Thr Ala Asp Val Ile Leu Arg Gly Tyr Ala Gly Trp
35 40 45

Asn Ser Arg Ser Ala Leu Lys Val Leu Asn Gln Val Phe Pro Lys Asp 50 55 60

Ala Val Ile Gln Pro Ser Leu Val Ile Val Tyr Phe Gly Gly Asn Asp 65 70 75 80

Ser Met Pro Pro His Pro Ser Gly Gln Gly Pro His Val Pro Leu Ser 85 90 95

Glu Phe Thr Glu Asn Met Arg Lys Ile Gly Glu His Leu Leu Ser Leu 100 105 110

Ser Asp Lys Thr Arg Val Ile Phe Leu Thr Pro Pro Pro Met Asn Glu 115 120 125

Arg Gln Ile Gln Leu Val Phe Gly Asp Ala Met Arg Gly Arg Ser Asn 130 135 140

Glu Leu Cys Arg Pro Tyr Ala Glu Ala Leu Leu Asn Leu Cys Arg Glu 145 150 160

Ile Asn Val Lys Gly Ile Asp Leu Trp Asn Ala Ile Gln Gln Gln Asp 165 170 175

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. 0 20								28/29								
Asp	Trp	Leu	His 180	Thr	Cys	Phe	Thr	Asp 185	Gly	Ile	His	Phe	Thr 190	Ala	Lys	

Ala Ser Glu Ile Val Val Lys Glu Ile Leu Lys Val Val Arg Glu Ala 195 200 205

Asp Trp Lys Pro Ser Leu Asp Arg Lys Ser Leu Pro Val Glu Phe Pro 210 215

Phe Asp Ser Gly Leu Pro Asn Ser Pro Arg His Ser Asp Leu Glu Leu 225 230 235 240

Thr Arg Asn Lys Lys Leu Glu Pro Arg Met Ala Arg Leu 245 250

<210> 27

<211> 651

<212> DNA

<213> Brassica napus

<220>

<221> CDS

<222> (1)..(261)

<223>

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ggc gcc gta ggt aaa acc tgt atg ctc atc tgc tac acc agc aac Gly Ala Val Gly Lys Thr Cys Met Leu Ile Cys Tyr Thr Ser Asn 20 25 30	aaa 96 Lys
ttc cct act gac tac ata cca aca gtt ttt gac aac ttt agt gca Phe Pro Thr Asp Tyr Ile Pro Thr Val Phe Asp Asn Phe Ser Ala 35 40 45	aac 144 Asn
gtt gta gtt gaa ggc acc act gtg aac cta ggc cta tgg gac act Val Val Glu Gly Thr Thr Val Asn Leu Gly Leu Trp Asp Thr 50 55 60	gct 192 Ala
ggg caa gaa gac tac aac aga tta agg cct tta agt tac aga gga Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly 65 70 75	gca 240 Ala 80
gat gtt ttc gtc ctg tct ttc tccttggtca gccgagctag ctacgagaa Asp Val Phe Val Leu Ser Phe 85	t 291
gtttataaaa agtggatccc tgaactccaa cactttgccc caggagttcc atta	gtcctt 351

gttggtacca aactagatct ccgtgaagat aataagcatt atttggctga ccatcctgga

411

ctatcccctg taactactgc acagggagag gaattgcgta agctaatcgg tgcgacatat 471
tacattgaat gtagctcgaa aactcaacag aatgtgaaag cagtttttga ttcagcgatc 531
aaggaagtga tcaaaccggt ggttaaacaa aaggagaaga cgcagaaaac gaagaagcaa 591
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<210> 28

<211> 87

<212> PRT

<213> Brassica napus

<400> 28

Met Ala Ser Thr Ala Ser Lys Phe Ile Lys Cys Val Thr Val Gly Asp 1 10 15

Gly Ala Val Gly Lys Thr Cys Met Leu Ile Cys Tyr Thr Ser Asn Lys 20 25 30

Phe Pro Thr Asp Tyr Ile Pro Thr Val Phe Asp Asn Phe Ser Ala Asn 35 40 45

Val Val Glu Gly Thr Thr Val Asn Leu Gly Leu Trp Asp Thr Ala 50 55 60

Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala 65 70 75 80

Asp Val Phe Val Leu Ser Phe 85

<210> 29

<211> 651

<212> DNA

<213> Brassica napus

<220>

<221> CDS

<222> (1)..(651)

<223>

<400> 29
atg get tea agt get tea aag tte ate aaa tgt gta aet gtt ggt gat

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							3	0/291	l					_	_	
Met 1	Ala	Ser	Ser	Ala 5	Ser	Lys	Phe	Ile	Lys 10	Cys	Val	Thr	Val	Gly 15	Asp	
ggt Gly	gcc Ala	gtt Val	ggt Gly 20	aaa Lys	acc Thr	tgt Cys	atg Met	ctc Leu 25	atc Ile	tgc Cys	tat Tyr	acc Thr	agc Ser 30	aac Asn	aag Lys	96
ttc Phe	cct Pro	act Thr 35	gac Asp	tat Tyr	gta Val	cca Pro	acg Thr 40	gtt Val	ttt Phe	gac Asp	aac Asn	ttt Phe 45	agt Ser	gca Ala	aac Asn	144
gtt Val	gta Val 50	gtt Val	gaa Glu	gga Gly	act Thr	act Thr 55	gtg Val	aac Asn	tta Leu	gjå aaa	cta Leu 60	tgg Trp	gat Asp	act Thr	gct Ala	192
gga Gly 65	caa Gln	gaa Glu	gac Asp	tat Tyr	aac Asn 70	aga Arg	tta Leu	agg Arg	cct Pro	tta Leu 75	agc Ser	tac Tyr	aga Arg	gga Gly	gca Ala 80	. 240
gat Asp	gtc Val	ttc Phe	gtc Val	ttg Leu 85	tct Ser	ttc Phe	tca Ser	ttg Leu	gtt Val 90	agc Ser	cga Arg	gct Ala	agc Ser	tac Tyr 95	gag Glu	288
aat Asr	gtt Val	ttt Phe	aaa Lys 100	Lys	tgg Trp	atc Ile	cct Pro	gaa Glu 105	ctc Leu	caa Gln	cac	ttt Phe	gct Ala 110	PIO	gga Gly	336
gtt Val	cca Pro	tta Lev 115	ı Val	ctt Leu	gtc Val	ggt Gly	acc Thr 120	гуs	tta Leu	gat Asp	ctc	cgt Arg 125	GIU	gat Asp	aag Lys	384
cat	tat Tyr 130	: Let	g gct 1 Ala	gad Asp	cat His	cct Pro 135	GTĀ	cta Leu	tcc Ser	cct Pro	gta Val 140		act Thr	gca Ala	cag Gln	432
gg G1 14	y Gli	g gag ı Glu	g ttg ı Lei	g cgt 1 Arg	aag Lys 150	Lev	att Ile	ggt Gly	gca Ala	aca Thr 155	TAT	tac Tyr	att Ile	gaa Glu	tgt Cys 160	480
ag Se	c tca r Se:	a aaa r Lya	a act	c caa c Glr 165	ı Glr	aat Asr	gto Val	aaa L Lys	gca Ala 170	ı val	ttt Phe	gat Asp	t tog Sei	g gca c Ala 17	a atc a Ile 5	528
aa Ly	g ga s Gl	a gt u Va	g ato 1 Ilo 18	e Lys	a ccg	g gtg Val	g cti L Lei	t aaa 1 Lys 18!	3 GTI	g aag n Lys	g ggo	c aag	g acc s Th:		g aaa s Lys	576
aa Ly	g aa s Ly	g aa s Ly 19	s Gl	a cag n Gl	g tçç n Se	g aat c Asi	cae n Hi: 20	s Hl	s Gl	g tgʻ y Cy:	t tta s Le	a to u Se 20	r vo	c gt n Va	t ttg l Leu	624
tg C <u>y</u>	t gg s Gl 21	y Ar	g at g Il	a gt e Va	g ac	c cg r Ar 21	g Hi	t tg s	<b>a</b>							651

<210> 30

<211> 216

<212> PRT

<213> Brassica napus

Met Ala Ser Ser Ala Ser Lys Phe Ile Lys Cys Val Thr Val Gly Asp 1 5 10 15

Gly Ala Val Gly Lys Thr Cys Met Leu Ile Cys Tyr Thr Ser Asn Lys 20 25 30

Phe Pro Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn 35 40 45

Val Val Val Glu Gly Thr Thr Val Asn Leu Gly Leu Trp Asp Thr Ala 50 55 60

Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala 65 70 75 80

Asp Val Phe Val Leu Ser Phe Ser Leu Val Ser Arg Ala Ser Tyr Glu 85 90 95

Asn Val Phe Lys Lys Trp Ile Pro Glu Leu Gln His Phe Ala Pro Gly
100 105 110

Val Pro Leu Val Leu Val Gly Thr Lys Leu Asp Leu Arg Glu Asp Lys 115 120 125

His Tyr Leu Ala Asp His Pro Gly Leu Ser Pro Val Thr Thr Ala Gln 130 135 140

Gly Glu Glu Leu Arg Lys Leu Ile Gly Ala Thr Tyr Tyr Ile Glu Cys 145 150 155 160

Ser Ser Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ser Ala Ile 165 170 175

Lys Glu Val Ile Lys Pro Val Leu Lys Gln Lys Gly Lys Thr Lys Lys 180 185 190

Lys Lys Gln Gln Ser Asn His His Gly Cys Leu Ser Asn Val Leu 195 200 205

Cys Gly Arg Ile Val Thr Arg His 210 215

<210> 31

<211> 606

<212> DNA

<213> Brassica napus

<221> CDS

<222> (1)..(606)

<223>

<400 atg		1	aca	aαa	tte	atc	aag	tat	ata	acq	qtc	gga	gat	gga	gct		48
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gtg Val	gly aaa	aag Lys	act Thr 20	tgt Cys	atg Met	ctg Leu	att Ile	tca Ser 25	tat Tyr	acc Thr	agc Ser	aat Asn	act Thr 30	ttt Phe	cct Pro		96
acg Thr	gat Asp	tac Tyr 35	gtt Val	ccg Pro	aca Thr	gtt Val	ttt Phe 40	gac Asp	aat Asn	ttc Phe	agt Ser	gcg Ala 45	aat Asn	gtg Val	gtg Val		144
gtc Val	gat Asp 50	gga Gly	agt Ser	act Thr	gtc Val	aac Asn 55	ctc Leu	ggc Gly	ctg Leu	tgg Trp	gat Asp 60	act Thr	gct Ala	Gly 999	cag Gln		192
gaa Glu 65	gat Asp	tat Tyr	aac Asn	agg Arg	ctt Leu 70	Arg	cct Pro	ttg Leu	agt Ser	tac Tyr 75	aga Arg	gga Gly	gca Ala	gat Asp	gtg Val 80		240
ttt Phe	tta Leu	ttg Leu	gca Ala	ttt Phe 85	tcc Ser	cta Leu	att Ile	agc Ser	aag Lys 90	gcc Ala	agt Ser	tac Tyr	gag Glu	aac Asn 95	att Ile	:	288
tac Tyr	aaa Lys	aag Lys	tgg Trp 100		ccg Pro	gag Glu	ctg Leu	aaa Lys 105	cat His	tat Tyr	gcg Ala	cct Pro	agc Ser 110	atc	ccc Pro		336
att Ile	gta Val	ctc Leu 115	Val	gga Gly	acc Thr	aag Lys	tta Leu 120	. Asp	ttg Leu	agg Arg	gat Asp	gac Asp 125	гу	cag Gln	ttc Phe		384
ttg Leu	aaa Lys 130	Asp	cat His	cca Pro	gga Gly	gca Ala 135	Ala	tca Ser	ata Ile	aca Thr	act Thr 140	: ATa	cag Gln	gga Gly	gag Glu		432
gaa Glu 145	Leu	aga Arg	aag J Lys	atg Met	att Ile 150	Gly	gco Ala	ato Ile	aag Lys	tac Tyr 155	тес	a gaa a Glu	tgo Cys	ago Ser	tcc Ser 160	,	480
aaa Lys	acc Thr	cag Glr	g cag n Glr	aat Asr 165	ı Val	aag Lys	a Ala	gtg Val	ttt Phe	ası	aca Thi	a gcg r Ala	g ato	e cgg	gta Val	•	528
gcg	tto Lei	g agg	g cct g Pro 180	Pro	aag Lys	gca Ala	a aag a Lys	g aag Lys 189	з Гу	g ata s Ile	a aaq e Ly:	g cca	ttg Lei 190	Arg	g acc g Thr		576
aaa Lys	aga Arg	s tca Se: 19	r Ar	a aca	tgo Cys	ttt Phe	tte Phe 20	e Phe	c taa	ā							606

<210> 32

<211> 201

<212> PRT

<213> Brassica napus

<400> 32

Met Ser Thr Ala Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala 1 5 10 15

Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro 20 25 30

Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val
35 40 45

Val Asp Gly Ser Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln 50 55 60

Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 65 70 75 80

Phe Leu Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Ile 85 90 95

Tyr Lys Lys Trp Leu Pro Glu Leu Lys His Tyr Ala Pro Ser Ile Pro 100 105 110

Ile Val Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe
115 120 125

Leu Lys Asp His Pro Gly Ala Ala Ser Ile Thr Thr Ala Gln Gly Glu 130 135 140

Glu Leu Arg Lys Met Ile Gly Ala Ile Lys Tyr Leu Glu Cys Ser Ser 145 150 155 160

Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Thr Ala Ile Arg Val 165 170 175

Ala Leu Arg Pro Pro Lys Ala Lys Lys Lys Ile Lys Pro Leu Arg Thr 180 185 190

Lys Arg Ser Arg Thr Cys Phe Phe Phe

<210> 33

<211> 636

<212> DNA

<213> Brassica napus

<220>

<221> CDS

<222> (1)..(636)

<223>

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gct Ala	Thr	acg Thr	Phe	atc Ile	aag Lys	tgc Cys	gtc Val	act Thr 25	gtt Val	ggc	gat Asp	gga Gly	gct Ala 30	gtg Val	ggc Gly	96 
aaa Lys	act Thr	tgt Cys 35	ctt Leu	ctt Leu	atc Ile	tcc Ser	tac Tyr 40	acc Thr	agc Ser	aac Asn	acc Thr	ttt Phe 45	cct Pro	act Thr	gat Asp	144
tat Tyr	gtt Val 50	cct Pro	aca Thr	gtg Val	ttc Phe	gac Asp 55	aac Asn	ttc Phe	agt Ser	gca Ala	aat Asn 60	gtt Val	cta Leu	gtc Val	gat Asp	192
ggc Gly 65	aaa Lys	acc Thr	gtc Val	aat Asn	ctt Leu 70	ggt Gly	ctt Leu	tgg Trp	gat Asp	act Thr 75	gct Ala	ggt Gly	caa Gln	gaa Glu	gat Asp 80	240
tac Tyr	aat Asn	agg Arg	ctt Leu	aga Arg 85	cca Pro	ttg Leu	agt Ser	tac Tyr	aga Arg 90	gga Gly	gca Ala	gat Asp	gtt Val	ttc Phe 95	att Ile	288
ctt Leu	gcc Ala	ttt Phe	tct Ser 100	ctt Leu	atc Ile	agc Ser	agg Arg	cct Pro 105	agc Ser	ttt Phe	gag Glu	aac Asn	att Ile 110	gct Ala	aaa Lys	336
aag Lys	tgg Trp	gtc Val 115	cct Pro	gag Glu	ctg Leu	cga Arg	cat His 120	tat Tyr	gcc Ala	cct Pro	aac Asn	gtg Val 125	cct Pro	att Ile	gtt Val	384
cta Leu	gtg Val 130	gga Gly	act Thr	aaa Lys	tta Leu	gat Asp 135	cta Leu	aga Arg	gag Glu	gat Asp	aag Lys 140	aag Lys	ttc Phe	cca Pro	atg Met	432
aac Asn 145	tat Tyr	cca	ggt Gly	gct	tgc Cys 150	Thr	atc Ile	tca Ser	aca Thr	gaa Glu 155	Gln	ggt Gly	caa Gln	gag Glu	cta Leu 160	480
aga Arg	aaa Lys	gag Glu	ata Ile	gga Gly 165	Ala	tta Leu	gca Ala	tat Tyr	ata Ile 170	Glu	tgc Cys	agc Ser	tca Ser	aaa Lys 175	aca Thr	528
caa Gln	cag Gln	aac Asn	gtg Val	. Lys	gcg Ala	gtg Val	ttt Phe	gat Asp 185	Ala	gcg Ala	ata Ile	aaa Lys	gta Val 190	. vai	cta Leu	576
cag Gln	cct Pro	cct Pro	Thr	aaa Lys	att Ile	aag Lys	aaa Lys 200	Glr	aag Lys	aga Arg	aga Arg	ttt Phe 205	Arg	tto Phe	tgc Cys	624
	gct Ala 210	Lev		1												636

<210> 34

<211> 211

<212> PRT

<213> Brassica napus

<400> 34

Met Ser Ala Ser Val Ala Ala Ala Ser Val Ser Thr Thr Thr Ala

1 5 10 15

Ala Thr Thr Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala Val Gly 20 25 30

Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro Thr Asp 35 40 45

Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Leu Val Asp 50 55 60

Gly Lys Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp 65 70 75 80

Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val Phe Ile 85 90 95

Leu Ala Phe Ser Leu Ile Ser Arg Pro Ser Phe Glu Asn Ile Ala Lys
100 105 110

Lys Trp Val Pro Glu Leu Arg His Tyr Ala Pro Asn Val Pro Ile Val

Leu Val Gly Thr Lys Leu Asp Leu Arg Glu Asp Lys Lys Phe Pro Met 130 135 140

Asn Tyr Pro Gly Ala Cys Thr Ile Ser Thr Glu Gln Gly Gln Glu Leu 145 150 155 160

Arg Lys Glu Ile Gly Ala Leu Ala Tyr Ile Glu Cys Ser Ser Lys Thr 165 170 175

Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val Val Leu 180 185 190

Gln Pro Pro Thr Lys Ile Lys Lys Gln Lys Arg Arg Phe Arg Phe Cys
195 200 205

His Ala Leu 210 WO 2005/014828 36/291

<210> 35

<211> 588

<212> DNA

<213> Brassica napus

<220>

<221> CDS

<222> (1)..(588)

<223>

<400 atg Met 1	200	5 gct Ala	tcg Ser	agg Arg 5	ttc Phe	ata Ile	aag Lys	tgt Cys	gtc Val 10	acc Thr	gtc Val	ggc Gly	gat Asp	ggt Gly 15	gcc Ala	48
gtc Val	gga Gly	aaa Lys	acc Thr 20	tgt Cys	atg Met	ctg Leu	atc Ile	tct Ser 25	tac Tyr	acg Thr	agc Ser	aac Asn	acc Thr 30	ttc Phe	cct Pro	96
acg Thr	gac Asp	tat Tyr 35	gta Val	cca Pro	act Thr	gtt Val	ttc Phe 40	gat Asp	aac Asn	ttc Phe	agt Ser	gct Ala 45	aat Asn	gtg Val	gtt Val	144
gtt Val	gat Asp 50	gjå aaa	aac Asn	act Thr	gtg Val	aat Asn 55	ctt Leu	ggc Gly	ttg Leu	tgg Trp	gat Asp 60	aca Thr	gct Ala	ggt Gly	caa Gln	192
gaa Glu 65	gac Asp	tat Tyr	aac Asn	agg Arg	tta Leu 70	aga Arg	cca Pro	ttg Leu	agt Ser	tac Tyr 75	cgt Arģ	ggt Gly	gcg Ala	gat Asp	gtc Val 80	240
ttc Phe	att Ile	ctt Leu	gct Ala	ttc Phe 85	tct Ser	ctt Leu	atc Ile	agc Ser	aaa Lys 90	gct Ala	agc Ser	tac Tyr	gag Glu	aat Asn 95	ata Ile	288
gct Ala	aag Lys	aag Lys	tgg Trp 100	Ile	cct Pro	gag Glu	ctc Leu	agg Arg 105	His	tat Tyr	gcc Ala	cct Pro	ggt Gly 110	val	cct Pro	336
att Ile	atc Ile	ctc Leu 115	Val	gga Gly	aca Thr	aaa Lys	ctc Leu 120	Asp	ctt Leu	cga Arg	gat Asp	gac Asp 125	гÃа	cag Gln	ttc Phe	384
ttc Phe	ata Ile 130	Asp	cac His	cct	ggt Gly	gca Ala 135	Val	ccg Pro	att Ile	agt Ser	act Thr 140	ASI	cag Gln	gga Gly	gag Glu	432
gaa Glu 145	Leu	aag Lys	aaa Lys	ctg Lev	ata Ile 150	Gly	tct Ser	ccg Pro	gct Ala	tac Tyr 155	TTE	gaa Glu	tgo Cys	agt Ser	tca Ser 160	480
aag Lys	acc Thr	cag Glr	cag Glr	aad Asi 165	ı Val	r aag Lys	gca Ala	ı gto ı Val	ttt Phe 170	e asi	gca Ala	a Ala	ata Ile	a aaa E Lys 175	gta Val	528
gtg Val	ctt Lei	cag 1 Glr	g cca n Pro 180	Pro	a aac o Lys	g caa s Glr	a aag a Lys	g aag s Lys 185	F Lys	g aas S Lys	a aaq s Lys	g aag s Lys	g aat s Asi 190	1 GT	tgt Y Cys	576

588

gtt ttc ttg tga Val Phe Leu 195

<210> 36

<211> 195

<212> PRT

<213> Brassica napus

<400> 36

Met Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala 1 5 10 15

Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro 20 25 30

Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val 35 40 45

Val Asp Gly Asn Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln 50 60

Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 65 70 75 80

Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Ile 85 90 95

Ala Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro
100 105 110

Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe
115 120 125

Phe Ile Asp His Pro Gly Ala Val Pro Ile Ser Thr Asn Gln Gly Glu 130 140

Glu Leu Lys Lys Leu Ile Gly Ser Pro Ala Tyr Ile Glu Cys Ser Ser 145 150 155 160

Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val 165 170 175

Val Leu Gln Pro Pro Lys Gln Lys Lys Lys Lys Lys Lys Asn Gly Cys 180 185 190

Val Phe Leu 195

<210>	37															
<211>	594	4														
<212>	DN	A														
<213>	Bra	assi	ica 1	napu	8											
<220>										٠						
<221>	CD	s														
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gtg gg Val G	gt a ly I	'Àa	aca Thr 20	tgt Cys	ctc Leu	ctc Leu	att Ile	tct Ser 25	tac Tyr	acc Thr	agc Ser	aac Asn	act Thr 30	ttc Phe	cct Pro	96
acg ga	sp 1	at Tyr 35	gtt Val	ccg Pro	act Thr	gtt Val	ttt Phe 40	gat Asp	aac Asn	ttc Phe	agc Ser	gct Ala 45	aat Asn	gtg Val	gtt Val	144
gtt aa Val Aa 5	sn G	gga 31y	gcc Ala	act Thr	gtc Val	aac Asn 55	ctt Leu	ggc Gly	ttg Leu	tgg Trp	gat Asp 60	acc Thr	gct Ala	GJA GGA	cag Gln	192
gag g Glu A 65	at t sp 1	tat Fyr	aac Asn	agg Arg	tta Leu 70	aga Arg	cca Pro	ttg Leu	agt Ser	tac Tyr 75	cgc Arg	ggt Gly	gct Ala	gat Asp	gtt Val 80	240
ttc a Phe I	tc t	tta Leu	gcc Ala	ttc Phe 85	tcc Ser	ctc Leu	atc Ile	agt Ser	aag Lys 90	gct Ala	agt Ser	tat Tyr	gag Glu	aat Asn 95	gtc Val	288
tcc a Ser L	ag a	aag Lys	tgg Trp 100	atc Ile	cct Pro	gag Glu	ctg Leu	act Thr 105	cac His	tat Tyr	gcc Ala	cct Pro	ggt Gly 110	gtc Val	cca Pro	336
att g Ile V	al :	ctt Leu 115	gtt Val	ggt Gly	acc Thr	aaa Lys	cta Leu 120	Asp	ctt Leu	agg Arg	gat Asp	gac Asp 125	aaa Lys	cag Gln	ttc Phe	384
ttc g Phe V	att ( /al .	gac Asp	cac His	cct Pro	ggt Gly	gct Ala 135	gta Val	cct Pro	att Ile	acc Thr	act Thr 140	gct Ala	cag Gln	gga Gly	gag Glu	432
gaa c Glu I 145	ctg Leu	atg Met	aag Lys	cta Leu	att Ile 150	gga Gly	gct	cct Pro	tcg Ser	tac Tyr 155	IIe	gag Glu	tgc Cys	agt Ser	tca Ser 160	480
aaa t Lys S	ca Ser	cag Gln	gag Glu	aac Asn 165	Val	aag Lys	GJ aaa	gtg Val	ttt Phe 170	Asp	gca Ala	gcg	att	aga Arg 175	var	528
gta d	ctt	caa	cct	cca	aag	cag	aag	, aaa	aag	aag	ggc	aaa	gta	caa	aag	576

WO 2005/014828 PCT/EP2004/008136

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Val Leu Gln Pro Pro Lys Gln Lys Lys Lys Gly Lys Val Gln Lys 180 185 190

gcc tgc tcc att ttg taa Ala Cys Ser Ile Leu 195 594

<210> 38

<211> 197

<212> PRT

<213> Brassica napus

·<400> 38

Met Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala 1 5 10 15

Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro 20 25 30

Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val 35 40 45

Val Asn Gly Ala Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln 50 55

Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 65 70 75 80

Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val 85 90 95

Ser Lys Lys Trp Ile Pro Glu Leu Thr His Tyr Ala Pro Gly Val Pro 100 105 110

Ile Val Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe 115 120 125

Phe Val Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly Glu 130 135 140

Glu Leu Met Lys Leu Ile Gly Ala Pro Ser Tyr Ile Glu Cys Ser Ser 145 150 155 160

Lys Ser Gln Glu Asn Val Lys Gly Val Phe Asp Ala Ala Ile Arg Val 165 170 175

Val Leu Gln Pro Pro Lys Gln Lys Lys Lys Gly Lys Val Gln Lys 180 185 190

Ala	Суз	Ser	Ile	Leu
		195		

<210> 39

<211> 645

<212> DNA

<213> Oryza sativa

<220>

<221> CDS

<222> (1)..(645)

<223>

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: Gly ggg	gac Asp	ggc Gly	gcg Ala 20	gtg Val	eja aaa	aag Lys	acg Thr	tgc Cys 25	atg Met	ctc Leu	atc Ile	tgc Cys	tac Tyr 30	acc Thr	tgc Cys	96
aac Asn	aag Lys	ttc Phe 35	ccc Pro	acc Thr	gat Asp	tac Tyr	atc Ile 40	ccc Pro	acc Thr	gtg Val	ttc Phe	gac Asp 45	aac Asn	ttc Phe	agc Ser	144
gcc Ala	aat Asn 50	gtc Val	tcc Ser	gtg .Val	gac Asp	ggg Gly 55	agc Ser	gtc Val	gtc Val	aac Asn	ctc Leu 60	ggc	ctc Leu	tgg Trp	gac Asp	192
act Thr 65	gca Ala	ggt Gly	cag Gln	gag Glu	gat Asp 70	tac Tyr	agc Ser	agg Arg	ttg Leu	agg Arg 75	cct Pro	ctg Leu	agc Ser	tac Tyr	agg Arg 80	240
gga Gly	gcc Ala	gat Asp	gtg Val	ttc Phe 85	atc Ile	ctg Leu	tcc Ser	ttc Phe	tcc Ser 90	ctg Leu	ata Ile	agc Ser	agg Arg	gcg Ala 95	agc Ser	288
tat Tyr	gag Glu	aat Asn	gtt Val 100	cag Gln	aag Lys	aag Lys	tgg Trp	atg Met 105	Pro	gag Glu	ctt Leu	cgc Arg	cgg Arg 110	Pne	gcg	336
cct Pro	ggt Gly	gtt Val 115	Pro	gta Val	gtt Val	ctt Leu	gtt Val 120	. Gly	acc Thr	aag Lys	ttg Leu	gat Asp 125	neu neu	cgt Arg	gaa Glu	384
gat Asp	agg Arg	Ala	tat Tyr	ctt Leu	gct Ala	gat Asp 135	His	cca Pro	gct Ala	tct Ser	tcc Ser 140	. TTE	ata : Ile	aca Thr	acg Thr	432
gag Glu 145	Glr	gly gga	gaa Glu	ı gaa ı Glu	cto Lev 150	ı Arg	aag Lys	g cta s Lev	ata l Ile	gga Gly 155	ATa	gto Val	gco L Ala	tao Tyr	atc Ile 160	480
gaa Glu	tgo Cys	ago Sei	tco Sei	aag Lys 165	Thi	a cag	g aga	a aac J Asr	att 11e 170	F PA	a gct s Ala	gtt Val	t tto L Phe	gad Asj 179	act Thr	528

					ctt Leu												576
aag Lys	aaa Lys	ctc Leu 195	caa Gln	tca Ser	agc Ser	tcc Ser	aat Asn 200	Arg	cca Pro	gta Val	agg Arg	cgg Arg 205	tac Tyr	ttt Phe	tgc Cys		624
			tgt Cys		gcg Ala	tag								٠.	•		645
_									٠.								
<210	)> 4	10												. •	•		
<21	L>2	214			٠		٠.										
<212	2> , 1	PRT												٠			
<213	3> (	oryza	a sat	iva													
:		•					•								٠		
<400	)	10															
							<b>~</b> 1	<b>3</b>	<b>5</b> 1	~1 ·	<b>.</b>	<b>~</b>	**- 7	<b>m</b> b	**- 1		
Met 1	Ser	Ser	Ala	Ala 5	Ala	Ala	Thr	Arg	Phe 10		гÀз	Cys	val	15	Val		-
Gly	Asp	Gly	Ala 20	Val	Gly	Lys	Thr	Сув 25	Met :	Leu	Ile	Cys	Tyr 30	Thr	Cys		
Asn	Lys	Phe 35	Pro	Thr	Asp	Tyr	Ile 40	Pro	Thr	Val	Phe	Asp 45	Asn	Phe	Ser		
Ala	Asn 50	Val	Ser	Val	Asp	Gly 55	Ser	Val	Val	Asn	Leu 60	Gly	Leu	Trp	Asp		
Thr 65	Ala	Gly	Gln	Glu	Asp 70	Tyr	Ser	Arg	Leu	Arg 75	Pro	Leu	Ser	Tyr	Arg 80		
Gly	Ala	Asp	Val	Phe 85	Ile	Leu	Ser	Phe	Ser 90	Leu	Ile	Ser	Arg	Ala 95	Ser		
Tyr	Glu	Asn	Val 100	Gln	Lys	Lys	Trp	Met 105	Pro	Glu	Leu	Arg	Arg 110	Phe	Ala.	•	
Pro	Gly	Val 115	Pro	Val	Val	Leu	Val 120	Gly	Thr	Lys	Leu	Asp 125	Leu	Arg	Glu		
Asp	Arg 130	Ala	Tyr	Leu	Ala	Asp 135	нis	Pro	Ala	Ser	Ser 140	Ile	Ile	Thr	Thr		
Glu 145	Gln	Gly	Glu	Glu	Leu 150	Arg	Lys	Leu	Ile	Gly 155	Ala	Val	Ala	Tyr	Ile 160		
Glu	Cys	Ser	Ser	Lys 165	Thr	Gln	Arg	Asn	Ile 170	Lys	Ala	Val	Phe	Asp 175	Thr	•	

432

Ala Ile Lys Val Val Leu Gln Pro Pro Arg His Lys Asp Val Thr Arg 180 185 190

Lys Lys Leu Gln Ser Ser Ser Asn Arg Pro Val Arg Tyr Phe Cys
195 200 205

Gly Ser Ala Cys Phe Ala 210

<210> 41

<211> 645

<212> DNA

<213> Oryza sativa

<220>

<221> CDS

<222> (1)..(645)

<223>

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gcc g Ala V	gtc Val	ggc Gly	aag Lys 20	acc Thr	tgc Cys	atg Met	ctc Leu	atc Ile 25	tgc Cys	tac Tyr	atc Ile	agc Ser	aac Asn 30	aag Lys	ttc Phe	96
ccc a	acc Thr	gat Asp 35	tac Tyr	atc Ile	ccc Pro	acc Thr	gtg Val 40	ttc Phe	gac Asp	aac Asn	ttc Phe	agt Ser 45	gct Ala	aat Asn	gtt Val	144
tca s	gtg Val 50	gat Asp	gly aaa	aac Asn	atc Ile	gtc Val 55	aac Asn	ttg Leu	gga Gly	tta Leu	tgg Trp 60	gac Asp	act Thr	gct Ala	gga Gly	192
caa Gln 65	gag Glu	gat Asp	tac Tyr	agc Ser	agg Arg 70	ctg Leu	agg Arg	cca Pro	ctg Leu	agc Ser 75	tac Tyr	agg Arg	gga Gly	gcg Ala	gat Asp 80	240
ata Ile	ttt Phe	gtg Val	ctg Leu	gca Ala 85	ttc Phe	tca Ser	ctg Leu	atc Ile	agc Ser 90	aga Arg	gca Ala	agc Ser	tat Tyr	gag Glu 95	aat Asn	288
gtt Val	ctc Leu	aag Lys	aag Lys 100	Trp	atg Met	ccg Pro	gag Glu	ctt Leu 105	cgc	cgg Arg	ttc Phe	gca Ala	ccg Pro 110	Wall	gtt Val	336
cca Pro	att Ile	gtt Val 115	Leu	gtt Val	gly	acc	aag Lys 120	Leu	gat Asp	cta Leu	. cgt . Arg	gac Asp 125	HIS	aga Arg	tct Ser	384

tac ctt gcg gac cat cct gct gct tcc gca att acg act gca cag ggt

Tyr Leu Ala Asp His Pro Ala Ala Ser Ala Ile Thr Thr Ala Gln Gly 135 gaa gaa ctt aga aag cag ata ggc gcc gcg gct tac atc gaa tgc agt 480 Glu Glu Leu Arg Lys Gln Ile Gly Ala Ala Ala Tyr Ile Glu Cys Ser tcg aaa aca caa cag aac atc aag gcc gtg ttt gat act gcc atc aag Ser Lys Thr Gln Gln Asn Ile Lys Ala Val Phe Asp Thr Ala Ile Lys 528 165 170 gtg gtc ctt cag cct cct cgg aga agg ggg gag acg acg atg gca agg 576 Val Val Leu Gln Pro Pro Arg Arg Gly Glu Thr Thr Met Ala Arg 180 185 aag aag aca agg cga agc acc ggc tgc tcg tta aag aac ttg atg tgt 624 Lys Lys Thr Arg Arg Ser Thr Gly Cys Ser Leu Lys Asn Leu Met Cys 645 ggc agt gca tgt gtt gtt tag Gly Ser Ala Cys Val Val 210

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<211> 214

<212> PRT

<213> Oryza sativa

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Ala Val Gly Lys Thr Cys Met Leu Ile Cys Tyr Ile Ser Asn Lys Phe 20 25 30

Pro Thr Asp Tyr Ile Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val 35 40 45

Ser Val Asp Gly Asn Ile Val Asn Leu Gly Leu Trp Asp Thr Ala Gly 50 55 60

Gln Glu Asp Tyr Ser Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp 65 70 75 80

Ile Phe Val Leu Ala Phe Ser Leu Ile Ser Arg Ala Ser Tyr Glu Asn 85 90 95

Val Leu Lys Lys Trp Met Pro Glu Leu Arg Arg Phe Ala Pro Asn Val

Pro Ile Val Leu Val Gly Thr Lys Leu Asp Leu Arg Asp His Arg Ser 115 120 125

Tyr	Leu Ala	Asp	His	Pro	Ala	Ala	Ser	Ala	Ile	Thr	Thr	Ala	Gln	Gly
•	130	_			135					140				

Glu Glu Leu Arg Lys Gln Ile Gly Ala Ala Ala Tyr Ile Glu Cys Ser 145 150 155 160

Ser Lys Thr Gln Gln Asn Ile Lys Ala Val Phe Asp Thr Ala Ile Lys 165 170 175

Val Val Leu Gln Pro Pro Arg Arg Gly Glu Thr Thr Met Ala Arg 180 185 190

Lys Lys Thr Arg Arg Ser Thr Gly Cys Ser Leu Lys Asn Leu Met Cys 195 200 205

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<220>

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ctc Leu	gtc Val	ctc Leu	ctc Leu 20	Gly ggc	gac Asp	GJÀ aaa	aga Arg	gta Val 25	ggc	aaa Lys	aca Thr	tct Ser	ctt Leu 30	gtg Val	ctg Leu	96
cgg Arg	tat Tyr	gtg Val 35	aat Asn	gat Asp	gtc Val	ttc Phe	tca Ser 40	gac Asp	aaa Lys	cag Gln	gaa Glu	gca Ala 45	act Thr	gtt Val	caa Gln	144
gct Ala	tca Ser 50	tat Tyr	ttg Leu	aca Thr	aag Lys	cgc Arg 55	ctt Leu	gtt Val	gtt Val	gaa Glu	ggt Gly 60	gtg Val	cct Pro	att Ile	acg Thr	192
ctc Leu 65	tct Ser	atc Ile	tgg Trp	gat Asp	aca Thr 70	gct Ala	gga Gly	caa Gln	gag Glu	aag Lys 75	ttc Phe	cat His	gca Ala	cta Leu	ggc Gly 80	240
cct Pro	ata Ile	tac Tyr	tat Tyr	cgt Arg 85	gat Asp	gca Ala	gac Asp	gct Ala	gct Ala 90	ctt Leu	tta Leu	gta Val	tat Tyr	gac Asp 95	atc Ile	288

Thr	gac Asp	aat Asn	gat Asp 100	Thr	ttt Phe	ctt Leu	cgt Arg	gtc Val 105	aca Thr	aag Lys	tgg Trp	gtg Val	aaa Lys 110	gag Glu	ctt Leu	
			Ala		aaa Lys											
					tca Ser											
					999 Gly 150											
ggt Gly	act Thr	Gly aaa	att Ile	gat Asp 165	gat Asp	atc Ile	ttc Phe	agt Ser	gac Asp 170	ata Ile	gcc Ala	aag Lys	aga Arg	tta Leu 175	tta Leu	
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					gtc Val											•
		tgc Cys		tag												•
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<21.	1> 2	212 .	٠													
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194

Thr Asp Asn Asp Thr Phe Leu Arg Val Thr Lys Trp Val Lys Glu Leu 100 105 110

Lys Gln Met Ala Asn Lys Asp Ile Val Met Ala Ile Ala Ala Asn Lys 115 120 125

Ser Asp Leu Val Arg Ser Lys His Ile Asp Thr Asn Glu Ala Ala Ser 130 135 140

Tyr Ala Glu Ser Ile Gly Ala Thr Leu Phe Val Thr Ser Ala Lys Ala 145 150 155 160

Gly Thr Gly Ile Asp Asp Ile Phe Ser Asp Ile Ala Lys Arg Leu Leu 165 170 175

Glu Arg Arg Lys Asn Ser Ser Asp Gly Leu Ser Leu Ala His Pro Lys 180 185 190

Lys Gly Ile Leu Ile Val Asp Asp Glu Pro Glu Lys Glu Pro Pro Pro 195 200 205

Lys Cys Cys Ser 210

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<213> Brassica napus

<220>

<221> CDS

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Pro Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val
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40
45

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		•								
VO 2005/014828 PCT/EP2004/008136										
	47/291									
Val Val Asn Gly Ala Thr Va 50	al Asn Leu Gly Leu Trp 55	Asp Thr Ala Gly 60								
cag gag gat tat aac aga to Gln Glu Asp Tyr Asn Arg Lo 65	eu Arg Pro Leu Ser Tyr									
gtt ttc atc tta gcc ttc to Val Phe Ile Leu Ala Phe So 80 85										
gtc tcc aag aag tgg atc co Val Ser Lys Lys Trp Ile P: 100										
cct att gtt ctt gtt gga ac Pro Ile Val Leu Val Gly Tl 115										
ttc ttc gtt gac cac cct g Phe Phe Val Asp His Pro G 130										
gag gaa cta atg aag cta at Glu Glu Leu Met Lys Leu I 145	t gga gct cct tcg tac le Gly Ala Pro Ser Tyr 50 155	Ile Glu Cys Ser								
tca aaa tca cag gag aac g Ser Lys Ser Gln Glu Asn V 160 165	ng aag ggg gtg ttt gat al Lys Gly Val Phe Asp 170	gca gcg atc aga 530 Ala Ala Ile Arg 175								
gtg gta ctt caa cct cca a Val Val Leu Gln Pro Pro L 180										
aag gcc tgc tcc att ttg t Lys Ala Cys Ser Ile Leu 195	gatttetet aegeteatet e	tettecaet 626								
ctctagtgaa ggcttaagaa gaa	gaaacac tttagccttt aag	atttggt tcagagttcg 686								
ttgtgataag cctcgcttaa tcc	tagaaa cgattacttc tgg	ttttact gataaagagc 746								
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<212> PRT

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<400> 46

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Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro 20 25 30

Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val 35 40 45

Val Asn Gly Ala Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln 50 55 60

Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 65 70 75 80

Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val 85 90 95

Ser Lys Lys Trp Ile Pro Glu Leu Thr His Tyr Ala Pro Gly Val Pro 100 105 110

Ile Val Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe 115 120 - 125

Phe Val Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly Glu 130 135 140

Glu Leu Met Lys Leu Ile Gly Ala Pro Ser Tyr Ile Glu Cys Ser Ser 145 150 155 160

Lys Ser Gln Glu Asn Val Lys Gly Val Phe Asp Ala Ala Ile Arg Val 165 170 175

Val Leu Gln Pro Pro Lys Gln Lys Lys Lys Lys Ser Lys Ala Gln Lys 180 185 190

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<210> 47

<211> 32

<212> PRT

<213> consensus

<220>

<221> MISC\_FEATURE

<222> (1)..(32)

<223> Xaa in position 15 is Leu, Ile or Met; Xaa in position 16 is Leu or Val; Xaa in position 17 is Ile, Leu or Tyr; Xaa in position 18 is Ser, Cys, Val or Arg; Xaa in position 20 is Thr, Ile or Val; Xaa in position 23 is Thr, Lys, Gln or Val

<400> 47

Lys Cys Val Thr Val Gly Asp Gly Ala Val Gly Lys Thr Cys Xaa Xaa

1

10

1.5

Xaa Xaa Tyr Xaa Ser Asn Xaa Phe Pro Thr Asp Tyr Val Pro Thr Val 20 25 30

<210> 48

<211> 32

<212> PRT

<213> consensus

<220>

<221> MISC FEATURE

<222> (1)..(32)

<223> Xaa any natural amino acid

<400> 48

Lys Xaa Val Xaa Xaa Gly Asp Xaa Xaa Xaa Gly Lys Xaa Xaa Xaa Xaa 1 10 15

Xaa Xaa Xaa Xaa Xaa Xaa Phe Xaa Xaa Xaa Xaa Xaa Xaa Thr Val

<210> 49

<211> 16

<212> PRT

<213> consensus

<220>

<221> MISC FEATURE

<222> (1)..(16)

<223>

<400> 49

Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu 1 5 10 15

<210> 50

<211> 16

<212> PRT

<213> consensus

<220>

<221> MISC\_FEATURE

<222> (1)..(16)

<223> Xaa in position 1 is Leu or Ile; Xaa in position 9 is Asp, Lys or Glu; Xaa in position 10 is Tyr or Phe; Xaa in position 11 is Asn, Ser, Ala, His or Glu; Xaa in position 12 is Arg or Ala; Xaa in position 14 is Arg, Ala or Gly; Xaa in position 16 is Leu, Ile or Phe

<400> 50

Xaa Trp Asp Thr Ala Gly Gln Glu Xaa Xaa Xaa Xaa Leu Xaa Pro Xaa 1 5 10 15

<210> 51

<211> 7

<212> PRT

<213> consensus

<400> 51

Gly Thr Lys Leu Asp Leu Arg

<210> 52

<211> 7

<212> PRT

<213> consensus

<220>

<221> MISC\_FEATURE

<222> (1)..(7)

<223> Xaa in postion 1 is Gly or Ala, Xaa in postion 2 is Thr, Asn or L eu, Xaa in postion 4 is Leu, Ala, Ser or Lys, Xaa in postion 7 is Arg, His or Val

<400> 52

Xaa Xaa Lys Xaa Asp Leu Xaa

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<211	.> 2	24															
<212	> I	ANC		•													
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					•	٠.								٠.		•	
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uog.	.ccgc		.55		-5	.55								•			
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																٠	
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	.> 57 !> Di	_				•					•			•			٠.
			romy	ces	cere	evisi	.ae							•			
<220	)> L> CI																
		L) :	(579)	+												•	
	> 59			:	_4.4.					~++	-++		aat.	~ a +	aat		48
Met 1	Ser	gaa Glu	Lys	gcc Ala 5	Val	aga Arg	Arg	Lys	Leu 10	Val	Ile	Ile	Gly	Asp 15	Gly		40
gct Ala	tgt Cys	ggc Glv	aag	acc	tot				10								
		2		Thr	Ser	Leu	cta Leu	Tyr	gta	ttt Phe	aca Thr	tta Leu	Gly	aaa Lys	ttc Phe		96
CCL	gaa	caa	20 tat	Thr	ser	Leu aca	Leu	Tyr 25 ttc	gta Val gag	Phe aat	Thr	Leu gtc	Gly 30 act	Lys gat	Phe tgc		96 14
Pro	Glu	caa Gln 35	20 tat Tyr	Thr cat His	ser ccg Pro	Leu aca Thr	Leu gtg Val 40	Tyr 25 ttc Phe	gta Val gag Glu	Phe aat Asn	Thr tat Tyr	Leu gtc Val 45	Gly 30 act Thr	Lys gat Asp	Phe tgc Cys		14
Pro aga	Glu gtt Val	caa Gln 35	20 tat Tyr	Thr cat His	ser ccg Pro	aca Thr gtg Val	Leu gtg Val 40 tcc	Tyr 25 ttc Phe tta	gta Val gag Glu acg	Phe aat Asn ctc	Thr tat Tyr tgg Trp	Leu gtc Val 45 gat	Gly 30 act Thr	Lys gat Asp gcg	Phe tgc Cys		
Pro aga Arg caa	Glu gtt Val 50 gag	caa Gln 35 gac Asp	20 tat Tyr gga Gly tat	Thr cat His ata Ile	Ser ccg Pro aaa Lys cgt	aca Thr gtg Val 55 tta	gtg Val 40 tcc ser	Tyr 25 ttc Phe tta Leu cca	gta Val gag Glu acg Thr	Phe aat Asn ctc Leu tca	tat Tyr tgg Trp 60 tat	Leu gtc Val 45 gat Asp	Gly 30 act Thr aca Thr	gat Asp gcg Ala gca	tgc Cys gga Gly		14
aga Arg caa Gln 65	gtt Val 50 gag Glu	caa Gln 35 gac Asp gaa Glu	20 tat Tyr gga Gly tat Tyr	Thr cat His ata Ile gaa Glu	Ser ccg Pro aaa Lys cgt Arg 70	Leu aca Thr gtg Val 55 tta Leu	Leu gtg Val 40 tcc ser cgt Arg	Tyr 25 ttc Phe tta Leu cca Pro	gta Val gag Glu acg Thr ttc Phe	Phe aat Asn ctc Leu tca ser 75	tat Tyr tgg Trp 60 tat Tyr	Leu gtc Val 45 gat Asp tca Ser	Gly 30 act Thr aca Thr aaa Lys	Lys gat Asp gcg Ala gca Ala	Phe tgc Cys gga Gly gat Asp 80		14· 19:
Pro aga Arg caa Gln 65 ata	Glu gtt Val 50 gag Glu ata	caa Gln 35 gac Asp gaa Glu	20 tat Tyr gga Gly tat Tyr	Thr cat His ata Ile gaa Glu ggg Gly	Ser CCG Pro aaa Lys CGt Arg 70 ttt	aca Thr gtg Val 55 tta	Leu gtg Val 40 tcc ser cgt Arg	Tyr 25 ttc Phe tta Leu cca Pro	gta Val gag Glu acg Thr ttc Phe	Phe aat Asn ctc Leu tca Ser 75 ttt	tat Tyr tgg Trp 60 tat Tyr	Leu gtc Val 45 gat Asp tca Ser	Gly 30 act Thr aca Thr aaa Lys	Lys gat Asp gcg Ala gca Ala att	Phe tgc Cys gga Gly gat Asp 80 aac		14
Pro aga Arg caa Gln 65 ata Ile	Glu gtt Val 50 gag Glu ata Ile	caa Gln 35 gac Asp gaa Glu tta Leu	20 tat Tyr gga Gly tat Tyr att Ile aaa Lys	Thr cat His ata Ile gaa Glu ggg Gly 85 tgg	Ser ccg Pro aaa Lys cgt Arg 70 ttt Phe	Leu aca Thr gtg Val 55 tta Leu gct	Leu gtg Val 40 tcc Ser cgt Arg gta Val	Tyr 25 ttc Phe tta Leu cca Pro gac Asp	gta Val gag Glu acg Thr ttc Phe aat Asn 90 tta	Phe aat Asn ctc Leu tca Ser 75 ttt Phe cga	tat Tyr tgg Trp 60 tat Tyr gaa Glu tat	Leu gtc Val 45 gat Asp tca Ser tca Ser	Gly 30 act Thr aca Thr aaa Lys cta Leu cct Pro	Lys gat Asp gcg Ala gca Ala att Ile 95 gac	Phe tgc Cys gga Gly gat Asp 80 aac Asn		14· 19:
Pro aga Arg caa Gln 65 ata Ile gca Ala cca	Glu gtt Val 50 gag Glu ata Ile agg Arg	caa Gln 35 gac Asp gaa Glu tta Leu acg Thr	20 tat Tyr gga Gly tat Tyr att Ile aaa Lys 100 ctt	Thr cat His ata Ile gaa Glu ggg Gly 85 tgg Trp	Ser CCG Pro aaa Lys CGt Arg 70 ttt Phe gCG Ala	Leu aca Thr gtg Val 55 tta Leu gct Ala gat	teu gtg Val 40 tcc ser cgt Arg gta Val gag Glu aaa Lys	Tyr 25 ttc Phe tta Leu cca Pro gac Asp gca Ala 105 aaa	gta Val gag Glu acg Thr ttc Phe aat Asn 90 tta Leu	Phe aat Asn ctc Leu tca Ser 75 ttt Phe cga Arg	tat Tyr tgg Trp 60 tat Tyr gaa Glu tat Tyr	Leu gtc Val 45 gat Asp tca Ser tca Ser tgt Cys caa Gln	Gly 30 act Thr aca Thr aaa Lys cta Leu cct Pro 110 gaa	Lys gat Asp gcg Ala gca Ala att Ile 95 gac Asp	Phe tgc Cys gga Gly gat Asp 80 aac Asn gca Ala		14· 19: 24· 28:
Pro aga Arg caa Gln 65 ata Ile gca Ala cca Pro	Glu gtt Val 50 gag Glu ata Ile agg Arg atc Ile aaa	caa Gln 35 gac Asp gaa Glu tta Leu acg Thr gtt Val 115 gag	20 tat Tyr gga Cly tat Tyr att Ile aaa Lys 100 ctt Leu	Thr cat His ata Ile gaa Glu ggg Gly 85 tgg Trp gta Val	Ser CCG Pro aaa Lys CGt Arg 70 ttt Phe GCG GCG acc	Leu aca Thr gtg Val 55 tta Leu gct Ala gat Asp ttg Leu gat	teu gtg Val 40 tcc Ser cgt Arg gta Val gag Glu aaa Lys 120 gaa	Tyr 25 ttc Phe tta Leu cca Pro gac Asp gca Ala 105 aaa Lys atg	gta Val gag Glu acg Thr ttc Phe aat Asn 90 tta Leu gat Asp	Phe aat Asn ctc Leu tca Ser 75 ttt Phe cga Arg ttg Leu ccc	tat Tyr tgg Trp 60 tat Tyr gaa Glu tat Tyr	Leu gtc Val 45 gat Asp tca Ser tca Cys caa Gln 125 gaa	Gly 30 act Thr aca Thr aaa Lys cta Leu cct Pro 110 gaa Glu gat	Lys gat Asp gcg Ala gca Ala att Ile 95 gac Asp gcc Ala	Phe tgc Cys gga Gly gat Asp 80 aac Asn gca Ala cat His aaa		14. 19: 24: 28:
Pro aga Arg caa Gln 65 ata Ile gca Ala cca Pro	Glu gtt Val 50 gag Glu ata Ile agg Arg atc Ile aaa	caa Gln 35 gac Asp gaa Glu tta Leu acg Thr gtt Val 115 gag	20 tat Tyr gga Cly tat Tyr att Ile aaa Lys 100 ctt Leu	Thr cat His ata Ile gaa Glu ggg Gly 85 tgg Trp gta Val	Ser CCG Pro aaa Lys CGt Arg 70 ttt Phe GCG GCG acc	Leu aca Thr gtg Val 55 tta Leu gct Ala gat Asp ttg Leu	teu gtg Val 40 tcc Ser cgt Arg gta Val gag Glu aaa Lys 120 gaa	Tyr 25 ttc Phe tta Leu cca Pro gac Asp gca Ala 105 aaa Lys atg	gta Val gag Glu acg Thr ttc Phe aat Asn 90 tta Leu gat Asp	Phe aat Asn ctc Leu tca Ser 75 ttt Phe cga Arg ttg Leu ccc	tat Tyr tgg Trp 60 tat Tyr gaa Glu tat Tyr	Leu gtc Val 45 gat Asp tca Ser tca Cys caa Gln 125 gaa	Gly 30 act Thr aca Thr aaa Lys cta Leu cct Pro 110 gaa Glu gat	Lys gat Asp gcg Ala gca Ala att Ile 95 gac Asp gcc Ala	Phe tgc Cys gga Gly gat Asp 80 aac Asn gca Ala cat His aaa		14· 19: 24: 28: 33:

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115					150		Ala	52/29 Lys	Lys	TDD						•		
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agt Ser	ttg Leu	ctt Leu	Met	165 aag Lys	aag Lys	gaa Glu	cca Pro	Gly 999	qct	aac Asn	tgt Cys	tgc Cys	ata Ile 190	att	tta Lei	1 3	5	576
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7			Lys	5				Tyr 25	10					13				
Pro	Glu	Gln	20 . Tyr	His	Pro	Thr	Val	Phe	Glu	Asn	Tyr	Val		Asp	Су	s		
_	50					55		Leu			60							
	Glu	Glu	Tyr	Glu	Arg	Leu	Arg	Pro	Phe	Ser	Туг	ser	. rys	Ala	A. A.S 80	p )		
				25	Phe			Asp	90					93				
			100	Tr				Ala 105	)				110	,				
		776	Lev	ı Val			120	Lys				123	,					
	72/	Gli	ı Ası			135		1 Met			14(	j						
	val	Ala	a Arg	g Ala	11e	Gly	Ala	Lys	Lys	з Туз 159	: Met	: Glı	1 Суя	s Se:	r A. 10	la 60		
145 Let	Th:	c Gly	y Gl		val	. Asp	Asp	va!	Phe 170	e Glı	ı Va	l Ala	a Thi	2 Ar	g T] 5	hr		
Sei	Le	ı Lei	1 Me		s Lys	s Glu	ı Pro	Gly 18	Ala		1 Су	з Су	s Ile 190	a Il		eu		
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tc Se	r Ar	g tt	t at le Il	c aa .e Ly	g tg s Cy	s Va	T TD	g gt r Va	t gg 1 G1	t ga .y As	t gg p Gl	y Ai	t gt .a Va	t gg	y I	aa Ys		105
Th	r Cy	rt ct	t tt	g at au Il	.e Se	r Ty	c ac	c ag r Se	c aa r As	at ac on Th	t tt ir Ph	c co	t ac	g ga	. بر	at Tyr 35		153
20 gt Va		c ac	et gt ir Va	al Pi	ie As	c aa	t tt n Ph	c ag ne Se	er Al	ca as La As	it qt	t gt al Va	t gt	c as	at o	199		201
ag Se	c ac r Th	et gt ir Va	cc aa al Aa 5!	sn Le	. a ac	g tt y Le	g to u Ti	gg ga cp As 60	p T	at a	et gg La G	ga ca ly G	ag ga ln Gl 65	ig ga	at t	tac Tyr		249

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								53/29	1.							-	
			_		_	_		_		_	_	_		att Ile	_		297
_					_		_	_				_		aag Lys	_		345
				_	_			_			_			gtt Val		٠	393
														ata Ile 130			441
			_						_	_				cta Leu			489
				_		_			_	_	_			aca Thr	caa Gln		537
_				_	-		_	_	_		_	Val	_	ctc Leu	cag Gln	•	585
	cct													tgc Cys	tcg Ser 195		. 633
	_	tgat	caaa	act o	gtagg	tcca	a co	gatag	gtgct	ggt	caca	att	ctc	gttgt	aa		689
teed	ctcac	ctc a	actc	tato	ec et	ttat	ctto	c ctt	cgto	ctca	gagg	gaagt	ac	gaggt	catc	<b>g</b> ,	749
tttg	tctt	at a	attt	gaaac	ct ac	taac	cato	t tqt	tgga	aat	atca	aggto	gc t	ttgg			803

<210> 58 <211> 197 <212> PRT

<213> Nicotiana tabacum

Met Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala 10 Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro 25 20 Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val .35 Val Asn Gly Ser Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 70 Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val 90 85 Ser Lys Lys Trp Ile Pro Glu Leu Lys His Tyr Ala Pro Gly Val Pro 100 105 Ile Val Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe 120 125 115 Phe Ile Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly Glu 135 140 Glu Leu Arg Lys Thr Ile Gly Ala Pro Ala Tyr Ile Glu Cys Ser Ser 150 155 Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val 165 170 175 Val Leu Gln Pro Pro Lys Thr Lys Lys Lys Gly Lys Ser Gln Lys 180 185 190 Ser Cys Ser Ile Leu 195

<210> 59 <211> 993 <212> DNA <213> Nicotiana tabacum <220> <221> CDS <222> (29)..(625) <400> 59 52 ggcacgaggg agatttgggt tttgtaga atg agt gcg tct agg ttc ata aag Met Ser Ala Ser Arg Phe Ile Lys tgt gtc acc gtt ggc gac gga gct gtg ggt aaa act tgt ctt ctc att 100 Cys Val Thr Val Gly Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile 15 20 148 tee tat ace age aac aca ttt cee act gat tac gte cea act gta tte Ser Tyr Thr Ser Asn Thr Phe Pro Thr Asp Tyr Val Pro Thr Val Phe 30 35 gac aat ttt agt gca aat gtg gtt gtc gat ggg agc act gtc aat ctg 196 Asp Asn Phe Ser Ala Asn Val Val Val Asp Gly Ser Thr Val Asn Leu 50 ggg ctg tgg gat act gca ggt cag gag gat tac aat aga tta aga ccg 244 Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro 65 ttg agc tac cgg ggg gca gat gta ttt ata ctg gca ttt tct ctc att 292 Leu Ser Tyr Arg Gly Ala Asp Val Phe Ile Leu Ala Phe Ser Leu Ile 85 80 age aaa geg age tat gaa aat gte tee aaa aag tgg att eet gaa ttg 340 Ser Lys Ala Ser Tyr Glu Asn Val Ser Lys Lys Trp Ile Pro Glu Leu 100 95 . 388 agg cat tat gct cct gga gtt cca att att ctt gtt gga aca aag cta Arg His Tyr Ala Pro Gly Val Pro Ile Ile Leu Val Gly Thr Lys Leu 110 gat ctc cga gag gat aag caa ttc ttc ctg gac cat cca ggt gct gtt 436 Asp Leu Arg Glu Asp Lys Gln Phe Phe Leu Asp His Pro Gly Ala Val 130 125 cca ctt acc aca gct cag ggt gaa gag ctg aga aag tcg att ggt gct 484 Pro Leu Thr Thr Ala Gln Gly Glu Glu Leu Arg Lys Ser Ile Gly Ala 145 150 140 tee get tae att gaa tgt agt gea aaa aca caa cag aat gtg aag get 532 Ser Ala Tyr Ile Glu Cys Ser Ala Lys Thr Gln Gln Asn Val Lys Ala 165 160 155 580 gtt ttt gat gct gcc att aag gtg gtt cta caa cca ccc aaa caa aag Val Phe Asp Ala Ala Ile Lys Val Val Leu Gln Pro Pro Lys Gln Lys 175 180 aag aaa aag aag aga aag ggt caa aaa gcc tgc tct atc ttg tgattgctga 632 Lys Lys Lys Lys Arg Lys Gly Gln Lys Ala Cys Ser Ile Leu 195 185 190 aataatagac aagtgatgga gatgtagatt gttatcaatg tettecaagt teaaagaatg 692 . cagtgtaagg ttcaacgttg gtagtcctga ctgactatga taggaaagca tgaatctgcc 752 ttgtccgtaa cattggaggc caagatgtat atttgtgatc cgcatatggt tggggataca 812 gatgtgcaaa attctctgtt tcgcgttgat tctgtgtaat atattatgta acacttgtgt 872 gatgatteet tgaatttgca tetaetatgt gttgttaaaa tgtaaccgaa catactgatt 932 992 993 a

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<211> 198
<212> PRT
<213> Nicotiana tabacum
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Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro
Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val
Val Asp Gly Ser Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln
Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val
                    70
Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val
                                    90
Ser Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro
                                105
Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Glu Asp Lys Gln Phe
                            120
Phe Leu Asp His Pro Gly Ala Val Pro Leu Thr Thr Ala Gln Gly Glu
                        135
                                            140
Glu Leu Arg Lys Ser Ile Gly Ala Ser Ala Tyr Ile Glu Cys Ser Ala
                    150
                                        155
Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val
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Val Leu Gln Pro Pro Lys Gln Lys Lys Lys Lys Lys Arg Lys Gly Gln
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Lys Ala Cys Ser Ile Leu
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<211> 640
<212> DNA
<213> Gossypium hirsutum
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                                                                       100
Gly Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser
aat act ttc cct acc gat tat gtg cca act gtc ttt gac aac ttt agt
                                                                       148
Asn Thr Phe Pro Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser
                        35
gct aat gtg gtt gtg gat ggg aac act gtt aat ctg gga ttg tgg gat
                                                                       196
Ala Asn Val Val Val Asp Gly Asn Thr Val Asn Leu Gly Leu Trp Asp
                    50
                                        55
act gct gga cag gaa gat tac aat aga tta aga cca ttg agc tat cgt
                                                                       244
Thr Ala Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg
gga gca gat gtc ttc ttg ctg gca ttt tct ctc att agc aaa gct agc
                                                                       292
Gly Ala Asp Val Phe Leu Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser
                                85
tat gaa aat gtt gct aag aaa tgg att cca gaa ttg aga cat tat gca
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Tyr Glu Asn Val Ala Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Ala
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56/291
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Pro Gly Val Pro Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Glu
                                           120
                       115
   110
gat aag cag ttc ttc ata gat cac cct ggt gcg gtg ccc att acc aca
                                                                      436
Asp Lys Gln Phe Phe Ile Asp His Pro Gly Ala Val Pro Ile Thr Thr
                                       135
                   130
gca cag ggt gag gaa ttg aga aag cta att gga gcg cat ttt tac att
                                                                      484
Ala Gln Gly Glu Glu Leu Arg Lys Leu Ile Gly Ala His Phe Tyr Ile
                                   150
                                                       155
               145
gag tgt agt tca aaa aca caa cag aat gtg aaa gcg gtc ttt gat gcg
Glu Cys Ser Ser Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala
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            160
gec ate aaa gta gtt ete eag eet eea aag aag aag aaa aag aag
                                                                      580
Ala Ile Lys Val Val Leu Gln Pro Pro Lys Lys Lys Lys Lys Lys
                                               185
                          180
aga aag gca caa aaa gct tgc tca ata ttg tgatcatgca aagaagtgat
Arg Lys Ala Gln Lys Ala Cys Ser Ile Leu
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<213> Gossypium hirsutum
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Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val
                            40
        35
Val Asp Gly Asn Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln
                        55
Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val
                                        75
                    70
Phe Leu Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val
                                    90
                85
Ala Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro
                                                    110
                               105
            100
Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Glu Asp Lys Gln Phe
                            120
Phe Ile Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly Glu
                                            140
                        135
Glu Leu Arg Lys Leu Ile Gly Ala His Phe Tyr Ile Glu Cys Ser Ser
                                                             160
                                        155
                    150
Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val
                                                        175
                                    170
                165
Val Leu Gln Pro Pro Lys Lys Lys Lys Lys Lys Arg Lys Ala Gln
                                185
            180
Lys Ala Cys Ser Ile Leu
        195
<210> 63
<211> 1025
<212> DNA
<213> Nicotiana tabacum
<220>
 <221> CDS
<222> (103)..(696)
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	agg Arg 5	ttt Phe	ata Ile	aaa Lys	tgt Cys	gtg Val 10	acg Thr	gtg Val	ggt Gly	gat Asp	ggt Gly 15	gcc Ala	gtt Val	gga Gly	aaa Lys	acg Thr 20		162
	tgt Cys	ctc Leu	ttg Leu	att Ile	tct Ser 25	tac Tyr	acc Thr	agc Ser	aac Asn	acc Thr 30	ttt Phe	Pro	acg Thr	gat Asp	tat Tyr 35	gtg Val		210
	Pro	Thr	Val	Phe 40	Asp	Asn	Phe	Ser	Ala 45	Asn	Val	Val	Val	Asn 50	Gly ggg	Ser		258
	Thr	Val	Asn 55	Leu	Gly	·Leu	Trp	Asp 60	Thr	Ala	Gly	Gln	Glu 65	Asp	tac Tyr	Asn		306
	Arg	Leu 70	Arg	Pro	Leu	Ser	Tyr 75	Arg	Gly	Ala	Asp	Val 80	Phe	Ile	ttg Leu	Ala		354
	Phe 85	Ser	Leu	Ile	Ser	Lys 90	Ala	Ser	Tyr	Glu	Asn 95	Val	Ser	ГÀз	aag Lys	Trp . 100		402
	Ile	Pro	Glu	Leu	Lys 105	His	Tyr	Ala	Pro	Gly 110	Val	Pro	Ile	Val	ctt Leu 115	Val	÷	450
	Gly	Thr	Lys	Leu 120	Asp	Leu	Arg	Asp	Asp 125	Lys	Gln	Phe	Phe	Ile 130		His		498
	Pro	Gly	Ala 135	Val	Pro	Ile	Thr	Thr 140	Ala	Gln	Gly	Glu	Glu 145	Leu	agg Arg	Lys		546
•	Thr	Ile 150	Gly	Ala	Pro	Ala	Tyr 155	Ile	Glu	Cys	Ser	Ser	Lys	Thr	caa Gln	Gln		594
	Asn 165	Val	Lys	Ala	Val	Phe 170	Asp	Ala	Ala	Ile	Lys 175	Val	Val	Leu	cag Gln	Pro 180		642
	Pro	Lys	Gln	Lys	Lys 185	Lys	Lys	Gly	Lys	Ala 190	Gln	ГÀЗ	Ala	Cys	tcg Ser 195	att Ile		690
	Leu			cag					*					•		. •		743
	ctc	tccc	tca	tatt	cctt	tg t	tttt	cett	t gt	ctcg	gaga	aag	tagg	agg	tcca	tgtatg		803
-	tct	cttt	aaa	atta	cttg	tg a	tctc	ttga	a tt	gcag	gtgg	ctc	ggtt	ttt	atac	tgetgt	•	863
	cat	ctct	agt	tgtt	gagt	ca c	agca	cctt	g tt	gtag	gcca	ctg	attg	ggc	cctc	tctggt		923
	ttc	attt	gct	ttat	gatt	aa t	gact	gaaa	g at	ccag	ttgg	aaa	aaaa	aaa	aaaa	aaaaaa		.983
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<210> 64 <211> 197

<212> PRT <213> Nicotiana tabacum

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58/291
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Val Asn Gly Ser Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln
                        55
Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val
                                        75
                    70
Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val
                85
Ser Lys Lys Trp Ile Pro Glu Leu Lys His Tyr Ala Pro Gly Val Pro
                                                    110
            100
                                105
Ile Val Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe
                                                125
                            120
        115
Phe Ile Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly Glu
                                             140
                        135
Glu Leu Arg Lys Thr Ile Gly Ala Pro Ala Tyr Ile Glu Cys Ser Ser
                                   155
                    150 ·
Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val
                                                         175
                                    170
                165
Val Leu Gln Pro Pro Lys Gln Lys Lys Lys Gly Lys Ala Gln Lys
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Ala Cys Ser Ile Leu
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 ataattaggt tegaa atg agt ggt tee agg tte ate aag tgt gte aca gtt
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                  Met Ser Gly Ser Arg Phe Ile Lys Cys Val Thr Val
 ggt gat ggt gcc gtt gga aag act tgt ttg ctt atc tcc tac acc agc
                                                                        219
 Gly Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser
                                                 25
                             20
         15
 aac act ttc cct acg gac tat gtg ccg act gtc ttt gac aat ttc agt
                                                                        267
 Asn Thr Phe Pro Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser
 gca aat gta gtt gtg gat ggg agc act ata aat ctc ggg ttg tgg gat
                                                                        315
 Ala Asn Val Val Val Asp Gly Ser Thr Ile Asn Leu Gly Leu Trp Asp
                                         55
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 act gct ggc caa gaa gat tac aat aga tta aga ccc tta agc tat cgt
                                                                        363
 Thr Ala Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg
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                 65
 gga gca gat gtt ttc ctg ctt gct ttt tct ctc ata agc aag gct agc
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 Gly Ala Asp Val Phe Leu Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser
                                 85
 tat gaa aat att gcc aaa aaa tgg att cct gag ttg agg cat tat gct
                                                                        459
 Tyr Glu Asn Ile Ala Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Ala
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 cct ggt gtt cca att att ctc gtt gga aca aaa ctt gat ctt cgg gat
 Pro Gly Val Pro Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp
                                              120
                         115
                                                                        555
 gat age cag tte ttt caa gae cat cet ggt geg geg eea ate ace aca
 Asp Ser Gln Phe Phe Gln Asp His Pro Gly Ala Ala Pro Ile Thr Thr
                                          135
 125
                      130
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gca cag ggt gag gaa ctg aga aaa ctt atc ggt gct cca gtt tac att Ala Gln Gly Glu Glu Leu Arg Lys Leu Ile Gly Ala Pro Val Tyr Ile 145 150 155	603
gaa tgt agt tcc aaa aca cag aag aat gtg aag gct gtt ttt gat tcg Glu Cys Ser Ser Lys Thr Gln Lys Asn Val Lys Ala Val Phe Asp Ser 160 165 170	651
gcc atc aaa gta gtt cta cag cca cca aag caa aag aaa aca aag aga Ala Ile Lys Val Val Leu Gln Pro Pro Lys Gln Lys Lys Thr Lys Arg 175 180	699
aag ggg caa aaa gcc tgt tcc att ttg tgatcttcag ttctttcgta Lys Gly Gln Lys Ala Cys Ser Ile Leu 190 195	746
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aaaaaaaaa aa	1178

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<212> PRT

<213> Medicago truncatula

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ener.

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Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val	
Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val .	
Ser Lys Lys Trp Ile Pro Glu Leu Lys His Tyr Ala Pro Gly Val Pro	
Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe	
115 120 125 Phe Val Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly Glu	
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tttgggtatt tcatttttca ag atg agt gct tct agg ttt att aaa tgt gtt Met Ser Ala Ser Arg Phe Ile Lys Cys Val 1 5 10	172
act gtt ggt gat gga gct gtt ggc aaa act tgt ttg ttg att tct tac Thr Val Gly Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr 15	220

								· · ·									
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ttc Phe	agt Ser	gcg Ala 45	aat	gtg Val	gtt <b>V</b> al	gtt Val	aat Asn 50	gga	agt Ser	att Ile	gtg Val	Asn	ctq	ggt Gly	ttg Leu		316
tgg Trp	gat Asp 60	act	gct Ala	gga Gly	caa Gln	gag Glu 65	gat	tat Tyr	aac Asn	aga Arg	tta Leu 70	55 aga Arg	cct Pro	ttg Leu	agt Ser		364
tac Tyr 75	cgt	ggt Gly	gcc Ala	gat Asp	gtt Val 80	ttc Phe	ata Ile	ttg Leu	gct Ala	ttc Phe 85	tct	ctc Leu	ata Ile	agc Ser	aaa Lys 90		412
gcc	agt Ser	tat Tyr	gaa Glu	aat Asn 95	gtc	tcc Ser	aaa Lys	aag Lys	tgg Trp 100	att	cca Pro	gag Glu	ttg Leu	aag Lys 105	cat His		460
tat Tyr	gca Ala	cct Pro	ggt Gly 110	gtc	CCC Pro	ata Ile	att	ctg Leu 115	gtt	gga Gly	aca Thr	aag Lys	ctt Leu 120	gat	ctt	•	508
						tgc Cys		gac					gtt			÷	556
acc Thr	aca Thr 140	gct	cag Gln	gga Gly	gaa Glu	gag. Glu 145	ctg	agg Arg	aag Lys	ctg Leu	att Ile 150	aat	gca Ala	cca Pro	gct Ala		604
tac Tyr 155	att	gaa Glu	tgc Cys	agt Ser	tca Ser 160	aaa Lys	tca Ser	cag Gln	Glu	aac Asn 165	gtg	aag Lys	gcg Ala	gtg Val	ttt Phe 170		652
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gaag	cata	ag g	rtggc	ttaa	t gt	tttt	gctt	tet	atga	att	atta	ttgt	ca a	ctct	aatag	•	933
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<211> 197

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<213> Medicago truncatula

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64/291	•
115 120 125	
Cys Ile Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly Glu 130 135 140	
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Lys Ser Gln Glu Asn Val Lys Ala Val Phe Asp Ala Ala Ile Arg Val 165 170 175	
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gct gtc gga aaa aca tgt ttg ttg att tct tac aca agc aac act ttc Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser Asn Thr Phe	275
cct acg gac tat gtg ccc acc gtt ttc gat aat ttc agt gct aat gtg Pro Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val	323
gtg gtt aac gga gcc acc gtt aat ctt gga ttg tgg gat act gca ggg Val Val Asn Gly Ala Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly	371
50 55 60  caa gag gat tac aac aga tta aga cca cta agc tac cgt gga gct gat Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp	419
65 70 70 75	467
Val Phe Ile Leu Ala Phe Ser Leu IIe Ser Lys Aid Sei Tyl Gid Abh	515
gtc tcc aaa aag tgg atc ccg gag ttg aag cat tac gcg cct ggt gtc Val Ser Lys Lys Trp Ile Pro Glu Leu Lys His Tyr Ala Pro Gly Val	313
and at at att and to and ott gat ctt cga gat gat aag caa	563
Pro Val Ile Leu Val Gly Ser Lys Leu Asp Leu Arg Asp Lys Gin	611
ttc ttc gtc gac cat cct ggc gct gtc ccg att aca act gct cag gga Phe Phe Val Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly 130 135 140	
gag gag ctg agg aag cta ata gat gca cct act tac atc gaa tgc agt Glu Glu Leu Arg Lys Leu Ile Asp Ala Pro Thr Tyr Ile Glu Cys Ser	659
tcc aaa tct caa gag aat gtg aaa gct gtc ttt gac gca gcc ata cga Ser Lys Ser Gln Glu Asn Val Lys Ala Val Phe Asp Ala Ala Ile Arg	707
160 165 170 173	
gtg gtg ttg caa ccg cct aag cag aag aag aaa aag agc aaa gcg cag Val Val Leu Gln Pro Pro Lys Gln Lys Lys Lys Ser Lys Ala Gln	755
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Lys Ala Cys Ser Ile Gln 195

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	70					75				Asp	80						
ttc	tct	ctc	atc	agt	aag	gct	agt	tat	gag	aat	gtc	tcc	aag	aag	rgg	463	
05					90					Asn 95					TOO		
a+0	cct	gag	ctg	acc	cac	tat	gcc	cct	ggt	gtc	cct	atc	gtt	ctt	gtt	511	•
Ile	Pro	Glu	Leu	Thr	His	Tyr	Ala	Pro	110	Val	Pro	TIE	vaı	115	Val		
ggt	acc	aaa	cta	gat	ctt	agg	gat	gac	aaa	cag	ttc	ttc	gtt	gac	cac	559	,
Gly	Thr	Lys	Leu 120	Asp	Leu	Arg	Asp	125	гЛа	Gin	Pue	Pne	130	Asp	HIS		_
cct	ggt	gct	gta	cct	att	acc	act	tct	cag	gga	gag	gaa	cta	atg	aag	607	7
Pro	Gly	Ala	Val	Pro	Ile	Thr	Thr 140	Ser	Gln	GTÅ	GIu	145	ьeu	Met	пур		_
cta	att	gga	gct	cct	tcg	tac	atc	gag	tgc	agt	tca	aaa	tct	caa	gag	65	Š
Leu	Ile	Gly	Ala	Pro	Ser	Tyr 155	Ile	Glu	Cys	Ser	Ser 160	ГÀЗ	ser	Gin	GIU.		_
aac	ata	aaa	ggg	gtg	ttt	gat	gca	gcg	atc	aga	gtg	gta	ctt	caa	cct	703	3
Asn	Val	Lys	Gly	Val	Phe	Asp	Ala	Ala	Ile	Arg	Val	Val	Leu	Gln	Pro 180		
165					170					175		~~~	+~~	+		75	1
cca	aag	cag	aag	aaa	aag	aag	agc	aag	gca	caa	Tare	gcc Ala	Cva	Ser	Tle	, 5.	-
Pro	Lys	Gln	Lys		ГÀЗ	гла	ser	тĀв	190	Gln	шуъ	ALG	Cys	195			
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Leu	taa																
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<210> 74 <211> 197 <212> PRT <213> Brassica napus

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<221> CDS <222> (1)..(645)

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Gly	Asp	Gly	Ala 20	Val	Gly	Lys	Thr	Cys 25	Met	Leu	atc Ile	Сув	Tyr	Thr	Cys		96
Asn	Lys	Phe 35	Pro	Thr	Asp	Tyr	Ile 40	Pro	Thr	Val	ttc Phe	Asp 45	Asn	Phe	Ser		144
Ala	Asn 50	Val	Ser	Val	Asp	Gly 55	Ser	Val	Val	Asn	ctc Leu 60	Gly	Leu	Trp	Asp		192
Thr 65	Ala	Gly	Gln	Glu	Asp 70	Tyr	Ser	Arg	Leu	Arg 75	cct Pro	Leu	Ser	Tyr	Arg	· • · •	240
Gly	Ala	Asp	Val	Phe 85	Ile	Leu	Ser	Phe	Ser	Leu	ata Ile	Ser	Arg	Ala 95	Ser		288
Tyr	Glu	Asn	Val 100	Gln	Lys	Lys	Trp	Met 105	Pro	Glu	ctt Leu	Arg	Arg 110	Phe	Ala		336
cct Pro	ggt	gtt Val 115	cct Pro	gta Val	gtt Val	ctt Leu	gtt Val 120	gga Gly	acc Thr	aag Lys	ttg Leu	gat Asp 125	ctc Leu	cgt Arg	gaa Glu		384
											tcc Ser 140						432
gag Glu 145	cag Gln	gga Gly	gaa Glu	gaa Glu	ctg Leu 150	agg Arg	aag Lys	cta Leu	ata Ile	gga Gly 155	gcg Ala	gtc Val	gcc Ala	tac Tyr	atc Ile 160	•	480
gaa Glu	tgc Cys	agc Ser	tcc Ser	aag Lys 165	aca Thr	cág Gln	aga Arg	aac Asn	att Ile 170	aaa Lys	gct Ala	gtt Val	ttc Phe	gac Asp 175	act Thr	•	528
Ala	Ile	Lys	Val 180	Val	Leu	Gln	Pro	Pro 185	Arg	His	aag Lys	Āsp	Val 190	Thr	Arg		576
aag Lys	Lys	ctc Leu 195	caa Gln	tca Ser	agc Ser	tcc Ser	aat Asn 200	cgg Arg	cca Pro	gta Val	agg Arg	cgg Arg 205	tac Tyr	ttt Phe	tgc Cys		624
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## WO 2005/014828 PCT/EP2004/008136

68/291 Pro Gly Val Pro Val Val Leu Val Gly Thr Lys Leu Asp Leu Arg Glu 125 120 Asp Arg Ala Tyr Leu Ala Asp His Pro Ala Ser Ser Ile Ile Thr Thr 135 140 130 Glu Gln Gly Glu Glu Leu Arg Lys Leu Ile Gly Ala Val Ala Tyr Ile 155 150 Glu Cys Ser Ser Lys Thr Gln Arg Asn Ile Lys Ala Val Phe Asp Thr 175 170 165 Ala Ile Lys Val Val Leu Gln Pro Pro Arg His Lys Asp Val Thr Arg 185 180 Lys Lys Leu Gln Ser Ser Ser Asn Arg Pro Val Arg Arg Tyr Phe Cys 195 200 Gly Ser Ala Cys Phe Ala 210 <210> 77 <211> 1135 <212> DNA <213 > Homo sapiens (man) <220> <221> CDS <222> (105)..(680) <400> 77 ggcagccgag gagaccccgc gcagtgctgc caacgccccg gtggagaagc tgaggtcatc 60 atcagatttg aaatatttaa agtggataca aaactatttc agca atg cag aca att 116 Met Gln Thr Ile aag tgt gtt gtt gtg ggc gat ggt gct gtt ggt aaa aca tgt ctc ctg 164 Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys Thr Cys Leu Leu 15 10 ata tee tae aca aca aac aaa ttt eea teg gaa tat gta eeg act gtt 212 Ile Ser Tyr Thr Thr Asn Lys Phe Pro Ser Glu Tyr Val Pro Thr Val 30 ttt gac aac tat gca gtc aca gtt atg att ggt gga gaa cca tat act Phe Asp Asn Tyr Ala Val Thr Val Met Ile Gly Gly Glu Pro Tyr Thr 260 40 ctt gga ctt ttt gat act gca ggg caa gag gat tat gac aga tta cga 308 Leu Gly Leu Phe Asp Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg 60 65 ccg ctg agt tat cca caa aca gat gta ttt cta gtc tgt ttt tca gtg 356 Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Val Cys Phe Ser Val 80 75 404 gto tot coa tot toa tit gaa aac gtg aaa gaa aag tgg gtg cot gag Val Ser Pro Ser Ser Phe Glu Asn Val Lys Glu Lys Trp Val Pro Glu 95 90 ata act cac cac tgt cca aag act cct ttc ttg ctt gtt ggg act caa 452 Ile Thr His His Cys Pro Lys Thr Pro Phe Leu Leu Val Gly Thr Gln 115 110 1.05 att gat etc aga gat gac ecc tet act att gag aaa ett gec aag aac 500 Ile Asp Leu Arg Asp Asp Pro Ser Thr Ile Glu Lys Leu Ala Lys Asn 130 120 125 aaa cag aag cct atc act cca gag act gct gaa aag ctg gcc cgt gac 548 Lys Gln Lys Pro Ile Thr Pro Glu Thr Ala Glu Lys Leu Ala Arg Asp 140 145 135 ctg aag gct gtc aag tat gtg gag tgt tct gca ctt aca cag aga ggt 596 Leu Lys Ala Val Lys Tyr Val Glu Cys Ser Ala Leu Thr Gln Arg Gly 160 155 ctg aag aat gtg ttt gat gag gct atc cta gct gcc ctc gag cct ccg 644 Leu Lys Asn Val Phe Asp Glu Ala Ile Leu Ala Ala Leu Glu Pro Pro 175 170 gaa act caa ccc aaa agg aag tgc tgt ata ttc taaactgttt tctccttccc 697 Glu Thr Gln Pro Lys Arg Lys Cys Cys Ile Phe 185 190

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	sapiens (ma				-	

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<400> 79

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<sup>&</sup>lt;213> Caenorhabditis elegans

<sup>&</sup>lt;220>

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<sup>&</sup>lt;222> (1)..(576)

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	1				5					10						tat		96	
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	Thr	Cys	Leu		Ile	Ser	Tyr	Thr	Thr	Asn	ALA	Pne	PIO	GIA	GIU	TYL			
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<213> Caenorhabditis elegans

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190

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<210> 82 <211> 192 <212> PRT

<213> Caenorhabditis elegans

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Glu L	ys T				Glu	Val	Arg	His 105	Phe	Cys	Pro	Asn	Val 110	Pro	Ile		
Ile L				Asn	Lys	Arg	Asp 120	Leu <sup>.</sup>	Arg	Ser	Asp	Pro 125	Gln	Thr	Val		
	30					135					140						
Arg A					150					155					160		
Ala L	_		_	165					170					175			
Ala A	la L		Gln 180	Gln	Lys	Lys	Lys	Lys 185	Lys	ser	rys	Cys	мет 190	iie	Leu		
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tgt c Cys L	Leu I	ett Leu 20	att Ile	tcc Ser	tat Tyr	act Thr	aca Thr 25	10 aac Asn	aag Lys	ttt Phe	cct Pro	agt Ser 30	gac	tat Tyr	gtg Val	153	
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cca t Pro 1	ac a	act Chr	ctt Leu	ggt Gly	tta Leu 55	ttc	gat Asp	acc Thr	gct Ala	ggt Gly 60	cag Gln	gag Glu	gat Asp	tat Tyr	gat Asp 65	249	
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gct o	Arg (	Glu	Leu	Gly 150	Ala	Val	. Гуз	Тух	Val 155	Glu	. Cys	Ser	· Ala	Leu 160	Thr	537	
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gat o Asp 1	Pro :	cct Pro 180	gtt Val	cct	cac His	aag Lys	aaa Lys 185	aag Lys	r tca	aag Lys	tgt Cys	tto Lev	ı Val	ctg Lev	[· L	630	
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ga	tttt	gcta	tac	tttt	get a	acatt	atto	gt al	tct	ctgo	c cat	tac	tcgc	agga	aattc		9:	28
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	Phe			· 85		* :			90				_	95	_			
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	3 > M		uscu	lus	(hou	se mo	ouse)	) .										
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	0> 85		, - , - ,				•			•								
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aag Lys	ccg Pro 50	gtg Val	aac Asn	ctg Leu	GJÅ 333	ctg Leu 55	tgg	gat Asp	acc Thr	gca Ala	ggt Gly 60	cag	gag Glu	gac Asp	tat Tyr		192	:
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<213> Mus musculus (house mouse)
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Į	tc éù 5	gct	ctc Leu	tgg Trp	gac Asp	acg Thr 60	gct Ala	gga Gly	cag Gln	gag Glu	gac Asp 65	tat Tyr	gac Asp	cgc Arg	ctg Leu	cga Arg 70		306	(
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<213> Discopyge ommata

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Asp Gly Lys Gln Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu
Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Thr Asp Val Ile
Leu Met Cys Phe Ser Ile Asp Ser Pro Asp Ser Leu Glu Asn Ile Pro
Glu Lys Trp Thr Pro Glu Val Lys His Phe Cys Pro Asn Val Pro Ile
                                  105
Ile Leu Val Gly Asn Lys Lys Asp Leu Arg Asn Asp Glu His Thr Arg
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Arg Glu Leu Ala Lys Met Lys Gln Glu Pro Val Lys Pro Thr Glu Gly
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Arg Asp Met Ala Asn Arg Ile Gly Ala Phe Gly Tyr Met Glu Cys Ser
Ala Lys Thr Lys Asp Gly Val Arg Glu Val Phe Glu Met Ala Thr Arg
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                                      170
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Leu
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                                                                          99
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                                          20
aat gcc ttt ccc ggc gag tac ata ccc acc gtg ttc gac aac tac tcg
                                                                          147
Asn Ala Phe Pro Gly Glu Tyr Ile Pro Thr Val Phe Asp Asn Tyr Ser
gcc aac gtg atg gtg gac gcc aag ccc atc aac ctg ggc ctg tgg gat
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Ala Asn Val Met Val Asp Ala Lys Pro Ile Asn Leu Gly Leu Trp Asp
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Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro
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Gln Thr Asp Val Phe Leu Ile Cys Phe Ser Leu Val Asn Pro Ala Ser
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caa	attt	taa	ataa	ctga	gt c	atca	cccci	t ct	gcac					atc   Ile			174
Cys	Val	Val	Val	Gly 10	Asp	gga Gly	Ala	Val	Gly 15	aag Lys	aca Thr	Сув	Leu	Leu 20	Ile		222
Ser	Tyr	Thr	Thr 25	Asn	Lys	ttc Phe	Pro	Ser	Glu	Tyr	Val	Pro	Thr	Val	Phe		270
qaA	Asn	Tyr 40	Alá	Väl	Thr	gtg Val	Met 45	Ile	Gly	Gly	Glu	Pro 50	Tyr	Thr	Leu	·• ·	318
Gly	Leu 55	Phe	Asp	Thr	Ala	gga Gly 60	Gln	Glu	Asp	Tyr	Asp 65	Arg	Leu	Arg	Pro		366
Leu 70	Ser	Tyr	Pro	Gln	Thr 75	gat Asp	Val	Phe	Leu	Val 80	Cys	Phe	Ser	Val	Val 85		414
Ser	Pro	Ser	Ser	Phe 90	Glu	aac Asn	Val	Lys	Glu 95	Lys	Trp	Val	Pro	Glu 100	Ile		462
Thr	His	Nis	Cys 105	Gln	Lys	acg Thr	Pro	Phe 110	Leu	Leu	Val	Gly	Thr 115	Gln	Ile		510
Asp	Leu	Arg 120	Asp	Glu	Asn	agc Ser	Thr 125	Leu	Glu	Lys	Leu	Ala 130	Lys	Asn	Lys	. *	·558
Gln	Lys 135	Pro	Ile	Thr	Met	gag Glu 140	Gln	Gly	Glu	ГÀа	Leu 145	Ala	Lys	Glu	Leu	• ·	606
Lys 150	Ala	Val	Lys	Tyr	Val 155	gag Glu	Cys	Ser	Ala	Leu 160	Thr	Gln	Lys	Gly	Leu 165		654
Lys	Asn	Val	Phe	Asp 170	Glu	gcc Ala	Ile	Leu	Ala 175	Ala <sub>.</sub>	Leu	Glu	Pro	Pro 180	Glu		702
Pro	Thr	Lys	Lys 185	Arg	Lys	cys	Lys	Phe 190	Leu					caca	ıc		752
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<212> PRT

<213> Drosophila melanogaster

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                                                 140
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                                                               15
                  5
                                         10
 tgt ggt aaa aca tgc tta tta att gta ttt tct aaa gga acc ttt ccc
                                                                               96
 Cys Gly Lys Thr Cys Leu Leu Ile Val Phe Ser Lys Gly Thr Phe Pro
                                     25
gag gtc tat gtt ccc act gtt ttt gaa aat tat gta gct gat gtt gag
                                                                               144
 Glu Val Tyr Val Pro Thr Val Phe Glu Asn Tyr Val Ala Asp Val Glu
                                40
          35
 gtt gat gga cgc cac gtt gag ttg gct ctt tgg gat acg gct gga caa
Val Asp Gly Arg His Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln
                                                                               192
                           55
  gaa gat tac gac cgt cta cgt ccc ttg tca tat cct gac tca cat gtt
                                                                               240
 Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Ser His Val
                        70
 atc ctt att tgc ttt gct gtt gat tct ccc gat tct ctt gac aat gtt
                                                                               288
 Ile Leu Ile Cys Phe Ala Val Asp Ser Pro Asp Ser Leu Asp Asn Val
 caa gaa aaa tgg att tcc gag gtt ctc cat ttc tgt tcc agt ctt cct
Gln Glu Lys Trp Ile Ser Glu Val Leu His Phe Cys Ser Ser Leu Pro
                                                                               336
                                     105
                                                           110
              100
  att ttg ctt gtc gct tgc aag gct gat ctc cgt aac gac cca aaa att
                                                                               384
  Ile Leu Leu Val Ala Cys Lys Ala Asp Leu Arg Asn Asp Pro Lys Ile
                                                      125
                                120
          115
  att gag gag tta tcc aag act aat cag cat ccc gtc acc aca gaa gaa
                                                                               432
  Ile Glu Glu Leu Ser Lys Thr Asn Gln His Pro Val Thr Thr Glu Glu
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      130
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 Gly Gln Ala Val Ala Gln Lys Ile Gly Ala Tyr Lys Tyr Leu Glu Cys
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                                              155
  tct gcc aag acg aat gaa ggt gtt cgt gag gtt ttt gaa tca gcc act
Ser Ala Lys Thr Asn Glu Gly Val Arg Glu Val Phe Glu Ser Ala Thr
                                                                               528
                                          170
                    165
  cgt gct gct atg ctc aaa cac aag ccc aaa gtg aag ccc tct agt gga
                                                                               576
  Arg Ala Ala Met Leu Lys His Lys Pro Lys Val Lys Pro Ser Ser Gly
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  act aag aag aag cgt tgt atc ttg ttg taa
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  Thr Lys Lys Lys Lys Arg Cys Ile Leu Leu
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<210> 96

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<sup>&</sup>lt;212> PRT

81/291 <213> Schizosaccharomyces pombe

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WO 2005/014828 PCT/EP2004/008136

82/291 Gln Gln Ala Glu Leu Val Ala Gln Arg Ile Gly Ala Arg Lys Tyr Met 150 155 gaa tgt tct tca ttg act ggt gac ggc gtg gac gat gta ttt gaa gct Glu Cys Ser Ser Leu Thr Gly Asp Gly Val Asp Asp Val Phe Glu Ala 528 170 165 qct act agg gca gca cta aca gtt cgg gat tcg gaa aat gac aag agt 576 Ala Thr Arg Ala Ala Leu Thr Val Arg Asp Ser Glu Asn Asp Lys Ser 180 185 tct aca aaa tgc tgc atc att tca taa 603 Ser Thr Lys Cys Cys Ile Ile Ser 195 <210> 98 <211> 200 <212> PRT <213> Schizosaccharomyces pombe Met Leu Gln Ser Gln Pro Ile Arg Arg Lys Leu Val Val Val Gly Asp 10 Gly Ala Cys Gly Lys Thr Ser Leu Leu Ser Val Phe Thr Leu Gly Tyr 25 20 Phe Pro Thr Glu Tyr Val Pro Thr Val Phe Glu Asn Tyr Val Ser Asp 45 40 Cys Arg Val Asp Gly Lys Ser Val Gln Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu Glu Tyr Glu Arg Leu Arg Pro Met Ser Tyr Ala Lys Ala 70 His Ile Ile Leu Val Gly Phe Ala Ile Asp Ser Pro Asp Ser Leu Glu 90 85 Asn Val Ser Thr Lys Trp Ile Glu Glu Ile Asn Thr Leu Cys Pro Asn 100 110 105 Val Pro Phe Ile Leu Val Gly Met Lys Ala Asp Leu Arg Ser Asp Pro 120 125 Val Ala Ile Glu Glu Met Arg Arg Arg Asn Gln Asn Phe Val Lys Ser 135 140 130 Gln Gln Ala Glu Leu Val Ala Gln Arg Ile Gly Ala Arg Lys Tyr Met 155 150 Glu Cys Ser Ser Leu Thr Gly Asp Gly Val Asp Asp Val Phe Glu Ala 170 175 165 Ala Thr Arg Ala Ala Leu Thr Val Arg Asp Ser Glu Asn Asp Lys Ser 185 190 180 Ser Thr Lys Cys Cys Ile Ile Ser 195 <210> 99 <211> 726 <212> DNA <213> Entamoeba histolytica <220> <221> CDS <222> (97)..(687) <400> 99 aaatqtaaaq aacattaaaa ataaaaaaac agtgaaaaga aatggattaa aaatagaatt 60 tcaaqqaact gaaactcgta attcaaaaga aaacac atg caa gct gtc aaa tgt 114 Met Gln Ala Val Lys Cys gtc att gtt ggg gat gga gct gta gga aaa act tgt ctt tta att tct 162 Val Ile Val Gly Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile Ser 15 tac act aca aat gca ttt cct aat gaa tat att cca aca gta ttt gat 210 Tyr Thr Thr Asn Ala Phe Pro Asn Glu Tyr Ile Pro Thr Val Phe Asp

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ьеи 55	Trp	Asp	Thr	A⊥a	eo GTÀ	Gln	Glu	Asp	Tyr	Asp 65	Arg	Leu		Pro	Leu		306
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Pro	Pro	Ser	Pne 90	Asp	Asn	Val	Ser	Ser 95	Lys	Trp	Gln	Pro	gaa Glu 100	Val	Ser	•	402
His	His	Cys 105	Pro	Lys	Thr	Pro	Cys 110	Leu	Leu	Val	Gly	Thr	aaa Lys	Leu	Asp		450
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135	Pro	Ile	Thr	Thr	Glu 140	Gln	Gly	Glu	Ala	Lys 145	Cys	Lys	gat Asp	Ile	Gly	. [	546
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Leu	Val	Phe	Asp 170	Glu	Ala	Val	Arg	Ala 175	Val	Ile	Ser	Pro	gca Ala 180	Gly	Gly	•	542
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<213> Entamoeba histolytica

<400> 100

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 Lys
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 Thr
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 Ile
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 Gly
 Asp
 Gly

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 Ala
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 Gly
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 Thr
 Cys
 Tyr
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 Thr
 Asn
 Glu
 Phe

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 Asp
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 Phe
 Asp
 Asn
 Tyr
 Val
 Val
 Ser
 Leu

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185

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Thr Val Leu

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195

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Met Ala Lys Glu Ile Lys Ala Val Lys Tyr Leu Glu Cys Ser Ala Leu
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165 170 175

Leu Thr Pro Pro Gln Thr Pro Gln Thr Arg Ala Lys Lys Ser Asn Cys 180 185 190

Thr Val Leu 195

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<221> CDS
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87/291
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                             120
                                                 125
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 Phe Val Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly Glu
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                                             140
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                                                          175
gtg ctg cag ccg cct aag gcg aag aag aaa aag gtg cag agg ggg
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                                 185
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Ala Cys Ser Ile Leu
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Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val
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Phe Leu Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val
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Ser Lys Lys Trp Ile Pro Glu Leu Lys His Tyr Ala Pro Gly Val Pro
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Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe
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Phe Val Asp His Pro Gly Ala Val Pro Ile Thr Thr Ala Gln Gly Glu
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                                             140
Glu Leu Arg Lys Gln Ile Gly Ala Pro Tyr Tyr Ile Glu Cys Ser Ser
                    150
                                        155
Lys Thr Gln Leu Asn Val Lys Gly Val Phe Asp Ala Ala Ile Lys Val
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Val Leu Gln Pro Pro Lys Ala Lys Lys Lys Lys Val Gln Arg Gly
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Ala Cys Ser Ile Leu
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ttcccgaggg accgagaaag ataagaaagg cggtggtcaa cttgtgtcct gaggtgcccg
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tagaagccca aggacaagaa acaaggagaa gagtagatct acatctactc caccg atg Met 1	178
agc gcg tct cgg ttc atc aag tgc gtc acc gtg ggg gac ggt gcc gtc Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala Val 5 10 15	226
gga aag acc tgc atg ctc atc tcc tac aca tcc aac act ttc ccc act Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro Thr 20 25 30	274
gac tat gtt cca act gtg ttc gac aac ttc agt gcc aat gtt gtg gtt Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val Val 35 40 45	322
gac ggg agc act gtc aac ttg ggt ctg tgg gat aca gca gga caa gaa Asp Gly Ser Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu 50 60 65	370
gat tac aat aga ctg cgt ccg ttg agc tat cgt ggt gct gat gtt ttt Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val Phe 70 75 80	418
ctg ctc gcc ttt tct ctt atc agc aaa gca agc tat gag aat gtc tct Leu Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val Ser 85 90 95	466
aag aag tgg gtt cct gaa tta agg cac tat gct cct ggc gtg ccc ata Lys Lys Trp Val Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro Ile 100 105 110	514
atc ctt gtt ggg aca aaa ctt gat ctg cgt gat gat aag cag ttt ttt Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe Phe 115 120 125	562
gtt gat cac cct ggt gct gtt cca att tcc act gcc cag ggc gaa gag Val Asp His Pro Gly Ala Val Pro Ile Ser Thr Ala Gln Gly Glu Glu 130 135 140	610
ctg agg aag cta att ggt gct gcc gcc tac atc gaa tgc agt tca aaa Leu Arg Lys Leu Ile Gly Ala Ala Ala Tyr Ile Glu Cys Ser Ser Lys 150 155 160	658
atc cag cag aac ata aaa gca gtg ttt gac gca gca att aag gtg gtt Ile Gln Gln Asn Ile Lys Ala Val Phe Asp Ala Ala Ile Lys Val Val 165 170 175	706
ctc cag cca cca aag caa aag aag aag aag aa	754
tgc acc att ttg taactacaaa cggtagaggg caacagtctg gctgcggcgc Cys Thr Ile Leu 195	806
tgetgecaat gataaceate geeteettge tgtataatat ategeetgat catgecaeca	866
gcatgcacaa gggagatggt ggttttagga teettgteet aetgtgttgt gtagaccace	926
gggtgtagtt gactgtatct ggttgtttgt atgtatggac aagacaaaac tagcactgca	986
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aaaaaaaaa aa	1058

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<sup>&</sup>lt;211> 197 <212> PRT

<sup>&</sup>lt;213> Zea mays (maize)

<sup>&</sup>lt;400> 108

Met Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala

Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro 25. Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val Val Asp Gly Ser Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val Phe Leu Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val Ser Lys Lys Trp Val Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro 100 105 Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe 120 Phe Val Asp His Pro Gly Ala Val Pro Ile Ser Thr Ala Gln Gly Glu 135 140 Glu Leu Arg Lys Leu Ile Gly Ala Ala Ala Tyr Ile Glu Cys Ser Ser 150 155 Lys Ile Gln Gln Asn Ile Lys Ala Val Phe Asp Ala Ala Ile Lys Val 165 170 Val Leu Gln Pro Pro Lys Gln Lys Lys Arg Lys Lys Val Gln Lys Gly Cys Thr Ile Leu 195 <210> 109 <211> 1045 <212> DNA <213> Zea mays (maize) <220> <221> CDS <222> (45)..(707) <400> 109 gaatteggea egagetgget egtgeagegg eggeagtgag ageg atg age geg 56 Met Ser Ala Ala gca gcg gcg gcg agc tcg gtc acc aag ttc atc aag tgc gtc acg Ala Ala Ala Ala Ser Ser Val Thr Lys Phe Ile Lys Cys Val Thr 104 15 gte gge gat ggg gee gte ggg aag ace tge atg etc ate tge tac ace 152 Val Gly Asp Gly Ala Val Gly Lys Thr Cys Met Leu Ile Cys Tyr Thr 30 tgc aac aag ttc ccc acg gat tac atc ccc acc gta ttt gac aac ttc 200 Cys Asn Lys Phe Pro Thr Asp Tyr Ile Pro Thr Val Phe Asp Asn Phe 45 age gee aat gte tee gtg ggt ggg age ate gte aac ttg gge ete tgg 248 Ser Ala Asn Val Ser Val Gly Gly Ser Ile Val Asn Leu Gly Leu Trp 60 65 gac acg gca ggc cag gag gat tac agc agg ttg agg cct ctc agc tac Asp Thr Ala Gly Gln Glu Asp Tyr Ser Arg Leu Arg Pro Leu Ser Tyr 296 agg ggt get gat gtg tte ate ete tee tte tee etg gte age agg geg 344 Arg Gly Ala Asp Val Phe Ile Leu Ser Phe Ser Leu Val Ser Arg Ala 95 age tat gag aac gtc ctg aag aag tgg atg cca gag ctt cgc cga ttt 392 Ser Tyr Glu Asn Val Leu Lys Lys Trp Met Pro Glu Leu Arg Arg Phe 110 tca cct act gtt cct gta gtt ctt gtt gga acc aaa cta gat ctc cgt Ser Pro Thr Val Pro Val Val Leu Val Gly Thr Lys Leu Asp Leu Arg 440 120 125 130 gaa gac aga tot tac ott got gac cat tot got got too atc atc tot 488 Glu Asp Arg Ser Tyr Leu Ala Asp His Ser Ala Ala Ser Ile Ile Ser 140 145 act gaa cag gga gaa gag ctc agg aag cag ata ggt gct gtg gcg tac 536 Thr Glu Gln Gly Glu Glu Leu Arg Lys Gln Ile Gly Ala Val Ala Tyr

	150					155					160					
			agc													584
Ile	Glu	Cys	Ser	Ser		Thr	Gln	Arg	Asn		Lys	Ala	Val	Phe		
165					170		•			175					180	
			aaa													632
Thr	Ala	Ile	Lys		Val	Leu	Gln	Pro		Arg	Arg	Arg	Glu		Thr	
				185					190					195		C00
															ctc	680
Arg	Lys	Lys	Met	гÀз	unr	ser	ser	Asn 205	GIN.	ser	ьeu	Arg	210	Tyr	Leu	
			200	+~+	++-	242	+~~			72 <i>0</i> 2	atat	-+a+a		atai	ttat's	734
			Gly					Laac	igcac	ay a	accc:	٠٠٠٠	gc 90	accy	ttgta	732
Cys	GIĀ	215	Gry	Cys	rne	1111	220									
ctac	ractt		.agat	taat.t	a ca	ageto		r aat	caaqt	tagt	ccc	ctcc	aca o	rcca	ctggga	794
005	,		5	-33-	- 5 - 1			,	JJ			•	•	•	- 3 3 3	
acti	cctgg	gtt d	ctct	gctad	ec ti	tacga	ataga	a gt	gatal	ttt	gcgt	ttcad	cca	gctga	agaaaa	 854
-			•			•							•			
atga	aagco	gag g	gttci	tagti	tt a	taaa	ttcc	c ta	cgag	gtgt	accı	ttcti	tta	gtate	gaatgg	914
<b>.</b>								~		-a++	atai	t a a a i	-~-		tttaas	974
rgg	getai	LLC 6	agcas	gulca	ag c	aaag	LgLg	ag	Lyaci		CLa	cycai	LyL	LLLY	tttcca	J14
aaaa	actas	ator 1	ttaci	taaai	ta a	ctaai	tgaai	ב ממי	ttato	arte	qca	ccaa	aaq a	aaaa	aaaaaa	1034
	5	5	3-		- 3 3		- 5	- ,33			J	33	-			
aaaa	aaaa	aaa a	a													1045

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<213> Zea mays (maize)

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..·

<210> 111

290

<211> 876 <212> DNA <213> Saccharomyces cerevisiae <220> <221> CDS <222> (1)..(876) <400> 111 atg aat aca cta tta ttt aag cga aaa ggt ggc aat tgt ggg aac gaa 48 Met Asn Thr Leu Leu Phe Lys Arg Lys Gly Gly Asn Cys Gly Asn Glu 10 agt aac ata gtt teg cag gga teg eec tea agt age aat ett eet gaa Ser Asn Ile Val Ser Gln Gly Ser Pro Ser Ser Asn Leu Pro Glu 20 25 tca cct ggc act tta gat gaa aag aat ctt ccc aga ttg cct act cca 144 Ser Pro Gly Thr Leu Asp Glu Lys Asn Leu Pro Arg Leu Pro Thr Pro 40 ttc gct aga agc ctt tct acc att cct agt tat gag cag atg aaa cgt 192 Phe Ala Arg Ser Leu Ser Thr Ile Pro Ser Tyr Glu Gln Met Lys Arg 55 aca aac aaa ctg cca gat tat cac cta aag att gtt gtt gtg gga gat 240 Thr Asn Lys Leu Pro Asp Tyr His Leu Lys Ile Val Val Gly Asp 70 75 ggc gct gta ggg aag acg tgc ctg ctg ata tct tat gtc caa gga aca 288 Gly Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Val Gln Gly Thr 90 ttt ccg act gat tat att cct act att ttc gaa aat tat gtc aca aac 336 Phe Pro Thr Asp Tyr Ile Pro Thr Ile Phe Glu Asn Tyr Val Thr Asn 100 105. ata gaa gga ccc aac ggt caa att ata gaa ttg gca tta tgg gac act 384 Ile Glu Gly Pro Asn Gly Gln Ile Ile Glu Leu Ala Leu Trp Asp Thr 120 gcc ggc caa gaa gag tat agt aga ctt aga ccg ctt tca tat acg aat 432 Ala Gly Gln Glu Glu Tyr Ser Arg Leu Arg Pro Leu Ser Tyr Thr Asn 130 135 140 gca gat gtg ctg atg gtg tgc tat tct gtt ggt agt aag aca tcg ctt Ala Asp Val Leu Met Val Cys Tyr Ser Val Gly Ser Lys Thr Ser Leu 480 .150 155 aaa aat gtg gaa gat ctc tgg ttc cca gag gtt aag cat ttt tgt cct 528 Lys Asn Val Glu Asp Leu Trp Phe Pro Glu Val Lys His Phe Cys Pro 170 175 tee act eea ate atg eta gte gge ett aaa tea gat eta tat gaa get 576 Ser Thr Pro Ile Met Leu Val Gly Leu Lys Ser Asp Leu Tyr Glu Ala 180 185 190 gat aac ctt tca gat ctg gtg gaa cca agt tca gca gaa tcc ttg gcc Asp Asn Leu Ser Asp Leu Val Glu Pro Ser Ser Ala Glu Ser Leu Ala 624 195 200 205 aag cgt ctg ggg gca ttt gca cat att caa tgc tca gca cga ttg aaa 672 Lys Arg Leu Gly Ala Phe Ala His Ile Gln Cys Ser Ala Arg Leu Lys 215 220 gaa aat atc gat gaa gta ttt gaa act gcc ata cac acg tta ctt tcc 720 Glu Asn Ile Asp Glu Val Phe Glu Thr Ala Ile His Thr Leu Leu Ser 235 gat toa tta tat got coc aga gag cot aca cat aca atc aaa aat coc 768 Asp Ser Leu Tyr Ala Pro Arg Glu Pro Thr His Thr Ile Lys Asn Pro 245 ttt aaa aga aat acc acc aga tca gat atc gat tct tct act gga gat 816 Phe Lys Arg Asn Thr Thr Arg Ser Asp Ile Asp Ser Ser Thr Gly Asp 260 265 270 acc age gte tet att tee gga aeg aaa aga tta aga aaa aac aag tgt 864 Thr Ser Val Ser Ile Ser Gly Thr Lys Arg Leu Arg Lys Asn Lys Cys 275 280 285 att ata atg taa .876 Ile Ile Met

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<213> Saccharomyces cerevisiae
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Ser Asn Ile Val Ser Gln Gly Ser Pro Ser Ser Ser Asn Leu Pro Glu
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            20
Ser Pro Gly Thr Leu Asp Glu Lys Asn Leu Pro Arg Leu Pro Thr Pro
                           40
Phe Ala Arg Ser Leu Ser Thr Ile Pro Ser Tyr Glu Gln Met Lys Arg
                                           60
                        55
Thr Asn Lys Leu Pro Asp Tyr His Leu Lys Ile Val Val Gly Asp
                                        75
                    70
Gly Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Val Gln Gly Thr
                                    90
                                                        95
                85
Phe Pro Thr Asp Tyr Ile Pro Thr Ile Phe Glu Asn Tyr Val Thr Asn
                                                    110
                               105
Ile Glu Gly Pro Asn Gly Gln Ile Ile Glu Leu Ala Leu Trp Asp Thr
                            120
                                               125
        115
Ala Gly Gln Glu Glu Tyr Ser Arg Leu Arg Pro Leu Ser Tyr Thr Asn
                        135
    130
Ala Asp Val Leu Met Val Cys Tyr Ser Val Gly Ser Lys Thr Ser Leu
                                        155
                    150
Lys Asn Val Glu Asp Leu Trp Phe Pro Glu Val Lys His Phe Cys Pro
                                    170
                165
Ser Thr Pro Ile Met Leu Val Gly Leu Lys Ser Asp Leu Tyr Glu Ala
                                185
                                                    190
Asp Asn Leu Ser Asp Leu Val Glu Pro Ser Ser Ala Glu Ser Leu Ala
                                                205
                            200
Lys Arg Leu Gly Ala Phe Ala His Ile Gln Cys Ser Ala Arg Leu Lys
                                           220
                        215
Glu Asn Ile Asp Glu Val Phe Glu Thr Ala Ile His Thr Leu Leu Ser
                                                            240
                                        235
                    230
Asp Ser Leu Tyr Ala Pro Arg Glu Pro Thr His Thr Ile Lys Asn Pro
                                    250
                                                        255
                245
Phe Lys Arg Asn Thr Thr Arg Ser Asp Ile Asp Ser Ser Thr Gly Asp
                                265
                                                    270
            260
Thr Ser Val Ser Ile Ser Gly Thr Lys Arg Leu Arg Lys Asn Lys Cys
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 Ile Ile Met
    290
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 <213> Saccharomyces cerevisiae
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 <221> CDS
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                                     10
 aga aag atc gtt att ttg ggc gac ggt gcc tgt ggt aaa act tcg ttg
                                                                       96
 Arg Lys Ile Val Ile Leu Gly Asp Gly Ala Cys Gly Lys Thr Ser Leu
                                 25
             20
 ctg aat gtt ttc acc aga ggt tat ttt ccc gaa gtt tat gag cct act
                                                                       144
 Leu Asn Val Phe Thr Arg Gly Tyr Phe Pro Glu Val Tyr Glu Pro Thr
                            40
                                                45
 gtt ttt gaa aac tat atc cat gat att ttc gtt gac agt aaa cat atc
                                                                       192
 Val Phe Glu Asn Tyr Ile His Asp Ile Phe Val Asp Ser Lys His Ile
```

			•						-	•							
								Gly ggc								•	240
cga		_				_	_	caa Gln	_	ata	-		-		agt Ser		288
	_		_	_			_	aat Asn 105	_					-			336
			Asp					gtc Val									384
	_	_		_			_	aat Asn	_			_			_		432
				_	_		_	gtt Val									480
		_						aac Asn	_		_		_	_			528
	_	_	_		_			gcg Ala 185		_		_	_	_	_		576
								gaa Glu									624
gtt Val								gca Ala									672
	tcc Ser		_			_	taa										696

<210> 114

<211> 231

<212> PRT

<213> Saccharomyces cerevisiae

Arg Ser Leu Ser Tyr Ser Asp Thr Gln Cys Ile Met Leu Cys Phe Ser 85 90 95

Ile Asp Ser Arg Asp Ser Leu Glu Asn Val Gln Asn Lys Trp Val Gly
100 105 110

Glu Ile Thr Asp His Cys Glu Gly Val Lys Leu Val Leu Val Ala Leu
115
120
125
Lug Cys Asp Nov Asp Asp Clu Asp Clu Sor Asp Ala Ile Thr Bro

Lys Cys Asp Leu Arg Asn Asn Glu Asn Glu Ser Asn Ala Ile Thr Pro 130 135 140

Asn Asn Ile Gln Gln Asp Asn Ser Val Ser Asn Asp Asn Gly Asn Asn 145 150 155 160

Ile Asn Ser Thr Ser Asn Gly Lys Asn Leu Ile Ser Tyr Glu Glu Gly 165 170 175

Leu Ala Met Ala Lys Lys Ile Gly Ala Leu Arg Tyr Leu Glu Cys Ser 180 185 190

Ala Lys Leu Asn Lys Gly Val Asn Glu Ala Phe Thr Glu Ala Ala Arg 195 200 205

Val Ala Leu Thr Ala Gly Pro Val Ala Thr Glu Val Lys Ser Asp Ser

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220
                         215
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Gly Ser Ser Cys Thr Ile Met
                    230
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<211> 579
<212> DNA
<213> Drosophila melanogaster
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atg acg acg att cgc aag aaa ttg gta att gtc ggc gac ggt gcc tgc
                                                                          48
Met Thr Thr Ile Arg Lys Lys Leu Val Ile Val Gly Asp Gly Ala Cys
                                      10
ggt aaa act tgc ctt ctg att gtc ttc agc aaa gat cag ttc ccc gag
                                                                          96
Gly Lys Thr Cys Leu Leu Ile Val Phe Ser Lys Asp Gln Phe Pro Glu
                                  25
             20
gtc tat gtg ccc acc gta ttc gag aat tat gtg gcc gac atc gag gtg
                                                                          144
Val Tyr Val Pro Thr Val Phe Glu Asn Tyr Val Ala Asp Ile Glu Val
                                                  45
                             40
gat ggc aaa cag gtg gag ctg gcc ttg tgg gat acg gcc ggg cag gag
Asp Gly Lys Gln Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu
                                                                          192
                         55
gac tac gac aga cta cga ccg ctg agc tat ccc gac act gac gtc ata
                                                                          240
Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Thr Asp Val Ile
                                          75
                     70
ctg atg tgt ttc tca gtg gat tca ccc gat tcg cta gaa aat att cct
                                                                          288
Leu Met Cys Phe Ser Val Asp Ser Pro Asp Ser Leu Glu Asn Ile Pro
                                                           95
gaa aaa tgg acc cca gag gtc aaa cac ttt tgt cca aat gtt cca atc
                                                                          336
Glu Lys Trp Thr Pro Glu Val Lys His Phe Cys Pro Asn Val Pro Ile
                                                       110
                                  105
             100
att ttg gta gga aat aag aaa gat ttg cga aat gat ccc aac aca att
                                                                          384
Ile Leu Val Gly Asn Lys Lys Asp Leu Arg Asn Asp Pro Asn Thr Ile
                             120
                                                   125
         115
 cgg gat cta gca aaa atg aag cag gag ccg gtg aag ccg cag gag ggt
                                                                          432
Arg Asp Leu Ala Lys Met Lys Gln Glu Pro Val Lys Pro Gln Glu Gly
                                               140
                          135
 cgc gcc atg gcc gag aag att aat gcc ttt gcc tat ttg gag tgt tcg
                                                                          480
Arg Ala Met Ala Glu Lys Ile Asn Ala Phe Ala Tyr Leu Glu Cys Ser
                                           155
                    . 150
 145
                                                                          528
 get aag tee aag gag ggt gtg ega gat gtt tte gag aeg gea aet agg
 Ala Lys Ser Lys Glu Gly Val Arg Asp Val Phe Glu Thr Ala Thr Arg
                                      170
                 165
 gec geg etg caa gte aaa aag agg aag aag ace aga tge ett ttg etc
                                                                          576
 Ala Ala Leu Gln Val Lys Lys Arg Lys Lys Thr Arg Cys Leu Leu Leu
                                   185
             180
                                                                           579
 taa
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<210> 116 <211> 192 <212> PRT

<213> Drosophila melanogaster

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Leu Met Cys Phe Ser Val Asp Ser Pro Asp Ser Leu Glu Asn Ile Pro
Glu Lys Trp Thr Pro Glu Val Lys His Phe Cys Pro Asn Val Pro Ile
             100
                                   105
Ile Leu Val Gly Asn Lys Lys Asp Leu Arg Asn Asp Pro Asn Thr Ile
                               120
Arg Asp Leu Ala Lys Met Lys Gln Glu Pro Val Lys Pro Gln Glu Gly
Arg Ala Met Ala Glu Lys Ile Asn Ala Phe Ala Tyr Leu Glu Cys Ser
                      150
                                            155
145
Ala Lys Ser Lys Glu Gly Val Arg Asp Val Phe Glu Thr Ala Thr Arg
                 165
                                        170
Ala Ala Leu Gln Val Lys Lys Arg Lys Lys Thr Arg Cys Leu Leu Leu
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Met Gln Ala lle Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys
                                                                              48
                                        10
acc tgc ctg ctg atc agc tac acg acc aat gcc ttt ccc ggc gag tac
                                                                              96
Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Ala Phe Pro Gly Glu Tyr
                                   25
ata ccc acc gtg ttc gac aac tac tcg gcc aac gtg atg gtg gac gcc Ile Pro Thr Val Phe Asp Asn Tyr Ser Ala Asn Val Met Val Asp Ala
                                                                              144
                               40
aag eec ate aac etg gge etg tgg gat aeg gee ggg eag gag gae tae
                                                                              192
Lys Pro Ile Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr
                           55
                                                 60
gac ega etg agg eca etg tee tat ece eag ace gat gte tte ete ate
                                                                              240
Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Ile
tgc ttc tcg ctg gtg aat ccg gca tcg ttc gag aac gtg cgg gca aag
                                                                              288
Cys Phe Ser Leu Val Asn Pro Ala Ser Phe Glu Asn Val Arg Ala Lys
tgg tat ccg gag gtg cgc cac cac tgc ccc agc acg ccc atc atc ctg Trp Tyr Pro Glu Val Arg His His Cys Pro Ser Thr Pro Ile Ile Leu
                                                                              336
                                   105
                                                                              384
gtg ggc acc aag ctg gat ttg cgc gac gac aag aac aca atc gaa aag
Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Asn Thr Ile Glu Lys
                               120
                                                     125
ctg agg gac aag aaa ctg gcg ccc atc acc tat ccg cag ggc tct ggc
                                                                              432
Leu Arg Asp Lys Leu Ala Pro Ile Thr Tyr Pro Gln Gly Ser Gly
                          135
                                                                              480
cat ggc aag gaa atc gga gcg gtc aag tat ctg gag tgc tcg gcc ctg
His Gly Lys Glu Ile Gly Ala Val Lys Tyr Leu Glu Cys Ser Ala Leu
acg cag aag ggt ctg aaa acc gtt ttc gac gag gcc atc cgg tcg gtt
                                                                              528
Thr Gln Lys Gly Leu Lys Thr Val Phe Asp Glu Ala Ile Arg Ser Val
                                        170
                                                             . 175
ttg tgc ccc gtg ctg cag ccc aag tcc aag cgc aag tgc gcc ctg ctc
                                                                              576
Leu Cys Pro Val Leu Gln Pro Lys Ser Lys Arg Lys Cys Ala Leu Leu
                                   185
                                                                              579
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<212> PRT
<213> Drosophila melanogaster
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                                25
            20
Ile Pro Thr Val Phe Asp Asn Tyr Ser Ala Asn Val Met Val Asp Ala
                            40
Lys Pro Ile Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr
                        55
                                            60
Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Ile
                    70
Cys Phe Ser Leu Val Asn Pro Ala Ser Phe Glu Asn Val Arg Ala Lys
                                     90
                85
Trp Tyr Pro Glu Val Arg His His Cys Pro Ser Thr Pro Ile Ile Leu
                                                    110
                                 105
            100
Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Asn Thr Ile Glu Lys
                                               125
                            120
        115
Leu Arg Asp Lys Lys Leu Ala Pro Ile Thr Tyr Pro Gln Gly Ser Gly
                                             140
                        135
His Gly Lys Glu Ile Gly Ala Val Lys Tyr Leu Glu Cys Ser Ala Leu
                                        155
                    150
Thr Gln Lys Gly Leu Lys Thr Val Phe Asp Glu Ala Ile Arg Ser Val
                                                         175
                                     170
                165
Leu Cys Pro Val Leu Gln Pro Lys Ser Lys Arg Lys Cys Ala Leu Leu
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<210> 119
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<212> DNA
<213> Drosophila melanogaster
<220>
 <221> CDS
 <222> (1)..(579)
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                                                                        48
 Met Gln Ala Ile Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys
                                     10
                5
 ace tgt ctg ctg atc agc tat acg acc aac gcc ttc ccc ggc gag tac
                                                                        96
 Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Ala Phe Pro Gly Glu Tyr
                                 25
             20
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 Ile Pro Thr Val Phe Asp Asn Tyr Ser Ala Asn Val Met Val Asp Ala
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 aag ccc atc aat ctg ggc ctc tgg gat acg gct gga cag gag gac tac
 Lys Pro Ile Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr
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 gat ege etg agg eeg eta tee tat eeg caa aeg gat gte tit ete ate
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 Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Ile
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 tgt ttc tca ctg gtg aat ccg gca tcg ttt gag aat gtg cga gcc aaa
 Cys Phe Ser Leu Val Asn Pro Ala Ser Phe Glu Asn Val Arg Ala Lys
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                 85
 tgg ttt ccc gag gtg cgt cat cat tgc ccg agt gtg ccg ata atc ctg
                                                                        336
 Trp Phe Pro Glu Val Arg His His Cys Pro Ser Val Pro Ile Ile Leu
                                 105
 gtc ggc acc aaa ctg gat ctg cgc gac gat aag cag acg atc gag aag
 Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Thr Ile Glu Lys
                                                 125
         115
                              120
                                                                        432
 ctg aag gac aag aag cta aca ccg atc acc tat ccc caa gga ctg gcg
 Leu Lys Asp Lys Lys Leu Thr Pro Ile Thr Tyr Pro Gln Gly Leu Ala
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97/291 135 140 atg gcc aag gaa ata gct gcg gtc aag tat ctg gag tgc tcg gcc ctg 480 Met Ala Lys Glu Ile Ala Ala Val Lys Tyr Leu Glu Cys Ser Ala Leu 145 150 155 acc caa aag ggt ctg aag acg gtc ttc gac gag gcc ata cga tcc gtg 528 Thr Gln Lys Gly Leu Lys Thr Val Phe Asp Glu Ala Ile Arg Ser Val 170 cta tgt cct gtc gtt cga gga ccc aag cgg cac aag tgc gcc ctg ctc 576 Leu Cys Pro Val Val Arg Gly Pro Lys Arg His Lys Cys Ala Leu Leu 185 taa 579 <210> 120 <211> 192 <212> PRT <213> Drosophila melanogaster <400> 120 Met Gln Ala Ile Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Ala Phe Pro Gly Glu Tyr Ile Pro Thr Val Phe Asp Asn Tyr Ser Ala Asn Val Met Val Asp Ala Lys Pro Ile Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Ile Cys Phe Ser Leu Val Asn Pro Ala Ser Phe Glu Asn Val Arg Ala Lys Trp Phe Pro Glu Val Arg His His Cys Pro Ser Val Pro Ile Ile Leu 105 Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Thr Ile Glu Lys 120 Leu Lys Asp Lys Leu Thr Pro Ile Thr Tyr Pro Gln Gly Leu Ala 135 Met Ala Lys Glu Ile Ala Ala Val Lys Tyr Leu Glu Cys Ser Ala Leu 150 155 Thr Gln Lys Gly Leu Lys Thr Val Phe Asp Glu Ala Ile Arg Ser Val 170 ' 165 Leu Cys Pro Val Val Arg Gly Pro Lys Arg His Lys Cys Ala Leu Leu 185 <210> 121 <211> 913 <212> DNA <213> Gossypium hirsutum (upland cotton) <220> <221> CDS <222> (12)..(602) <400> 121 gagaaaaaac a atg agc act gca aga ttt atc aag tgt gtc acg gtc ggt Met Ser Thr Ala Arg Phe Ile Lys Cys Val Thr Val Gly 10 gat gga get gtg ggg aaa act tgt atg etc att tea tat acc age aat Asp Gly Ala Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Ser Asn

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								98/29							~~~	242
Ala	Gly ggg	Gln	Glu 65	Asp	Tyr	Asn	Arg	Leu 70	Arg	Pro	Leu	ser	75	Arg	GLY	242
gct Ala	gat Asp	gtg Val 80	ttt Phe	ttg Leu	ttg Leu	gcc Ala	ttt Phe 85	tct Ser	ctt Leu	ata Ile	agc Ser	aag Lys 90	gcc Ala	agt Ser	tat Tyr	290
gaa Glu	aac Asn 95	atc	tac Tyr	aaa Lys	aag Lys	tgg Trp 100	atc Ile	cca Pro	gag Glu	cta Leu	aga Arg 105	cat His	tat Tyr	gct Ala	cat His	338
aat Asn 110	gta Val	cca Pro	gtt Val	gtg Val	ctt Leu 115	gtt Val	gga Gly	acc Thr	aaa Lys	cta Leu 120	gat Asp	ttg Leu	cga Arg	gat Asp	gac Asp 125	386
aaσ	cag Gln	ttc Phe	ctc Leu	att Ile 130	gat	cac His	cct Pro	gga Gly	gca Ala 135	aca Thr	cca Pro	ata Ile	tca Ser	aca Thr 140	tct Ser	434
cag Gln	gga Gly	gaa Glu	gaa Glu 145	cta	aag Lys	aag Lys	atg Met	ata Ile 150	Gly	gca Ala	gtt Val	act Thr	tat Tyr 155	TTE	gaa Glu	482
tgc Cys	agc Ser	tcc Ser 160	aaa	acc Thr	caa Gln	cag Gln	aat Asn 165	gtg Val	aag Lys	gct Ala	gtt Val	ttc Phe 170	Asp	gct Ala	gca Ala	530
ata Ile	aaa Lys 175	ota	gct Ala	ttg Leu	agg Arg	cca Pro 180	cca Pro	aaa Lys	cca Pro	aag Lys	aga Arg 185	гÀг	cct Pro	tgc Cys	aaa Lys	578
Arg	aga Arg	aca Thr	tgt Cys	gct Ala	ttc Phe 195	ctt Leu	tga	atat	tgg	atca	ttat	ta c	agtc	aaaa	a	629
190 cag	ttaa	caa	aagc	tgtt	gc a	gata	aaca	c tg	aatc	tgct	ata	gttt	gtt	tttg	gtttac	689
ata	tgtt	cca	cgtg	aaac	ta t	gaag	catc	t ct	aaga	aaac	cca	aact	atc	atat	caaccc	749
ato	gato	aat	gaat	cgat	tt c	aatt	ttcg	c ag	rtata	.agtt	cct	ttta	atc	cttt	ctttt	809
act	tcat	ttt	ataa	cgaa	tt c	tatg	gata	a to	rttcc	ctac	aaa	cato	rtca	ttac	aatgtt	869
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Glu Leu Lys Lys Met Ile Gly Ala Val Thr Tyr Ile Glu Cys Ser Ser 150 155 Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val 170 Ala Leu Arg Pro Pro Lys Pro Lys Arg Lys Pro Cys Lys Arg Arg Thr 185 Cys Ala Phe Leu 195 <210> 123 <211> 1067 <212> DNA <213> Arabidopsis thaliana (mouse-ear cress) <220> <221> CDS <222> (314)..(907). <400> 123 cttttctctc tctagttgtt gttctctctc tctctcgcat cctccaattc atcgtcctca 60 egtteeettt tgtttattea tetteettee ttetteacat ttetgatttt etetatttgg 120 ggggtttgtt tccacattat acatatctag ggttttgaga tggttaattg aaagataatg 180 gtcgaagttt cggaggaatt ggcttcacat tgtgggtgtt tctggcttcc tcaggtttaa 240 atctgaggtt gatctctttt gttttttggt aaattgtgac atattttggc tcgaagaaga 300 agaagaagag gca atg agc gca tca agg ttc ata aag tgc gtc acc gtt 349 Met Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val 397 ggt gat gga gct gtt ggt aaa acc tgt ttg ctg att tet tat acc agc Gly Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser aac acc ttt ccc acg gat tat gtt ccg act gtt ttc gat aac ttt agt 445 Asn Thr Phe Pro Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser 35 gca aat gtg gtt gtc aat ggg gcc acg gtg aat ctt gga ttg tgg gat Ala Asn Val Val Val Asn Gly Ala Thr Val Asn Leu Gly Leu Trp Asp 493 50 act gca ggg caa gag gac tat aac agg tta aga cct ttg agt tac cgt 541 Thr Ala Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg ggt gct gat gtt ttc att ctt gcc ttc tct ctc att agt aag gct agt 589 Gly Ala Asp Val Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser tat gag aat gtt tcc aag aag tgg att cca gag ttg aag cac tat gct 637 Tyr Glu Asn Val Ser Lys Lys Trp Ile Pro Glu Leu Lys His Tyr Ala 100 105 cct ggt gtc cca att gtc ctt gtt gga acc aaa cta gat ctt cga gat 685 Pro Gly Val Pro Ile Val Leu Val Gly Thr Lys Leu Asp Leu Arg Asp 115 120 733 gac aaa cag ttt ttc atc gac cat cct ggt gct gtc cct att acc act Asp Lys Gln Phe Phe Ile Asp His Pro Gly Ala Val Pro Ile Thr Thr 130 135 gtt cag gga gag gag ctg aag aag cta att gga gcg cca gct tac atc 781 Val Gln Gly Glu Glu Leu Lys Lys Leu Ile Gly Ala Pro Ala Tyr Ile gag tgc agt tca aaa tca caa gag aac gtg aag ggc gtg ttt gat gca 829 Glu Cys Ser Ser Lys Ser Gln Glu Asn Val Lys Gly Val Phe Asp Ala 165 170 gcg atc aga gtg gtc ctt caa cct cca aag cag aag aaa aag aac 877

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Ala Ile Arg Val Val Leu Gln Pro Pro Lys Gln Lys Lys Lys Asn 175 180 185	204
aaa gca caa aag gcc tgc tcc atc ttg taatagcact catggaagtc Lys Ala Gln Lys Ala Cys Ser Ile Leu 190	924
aagaagetet ttgagatgag gatgacaggg tggtttaaaa aagtateget ttttcatttt	984
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Val Asn Gly Ala Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln	
Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val	
Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val	
Ser Lys Lys Trp Ile Pro Glu Leu Lys His Tyr Ala Pro Gly Val Pro 100 105 110	
Ile Val Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe 115 120 125	
Phe Ile Asp His Pro Gly Ala Val Pro Ile Thr Thr Val Gln Gly Glu 130 135 140 130 135 140 130 130 130 130 130 130 130 130 130 13	
Glu Leu Lys Lys Leu Ile Gly Ala Pro Ala Tyr Ile Glu Cys Ser Ser 145 150 155 160 Lys Ser Gln Glu Asn Val Lys Gly Val Phe Asp Ala Ala Ile Arg Val	
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gtt ggt aaa acc tgt ttg ctg att tct tac acc agc aac act ttt cct Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro	96
acg gat tat gta ccg act gtt ttc gat aac ttt agc gca aat gtg gtt Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val 35 40 45	144

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					tta Leu 70 .												240
					tct Ser												288
					cca Pro											•	336
	Val				acc Thr											•	384
					ggc Gly											· :	432
					att Ile 150											•	480
					gtg Val												528
_					aag Lys	_	_		_		_		_				576
_	tgc Cys			_	taat	ttct	cct a	acgct	tct	et ta	acgta	tcto	e tet	ctgt	cete		631
tate	gtcto	ett d	ccact	cetto	et ag	gtgaa	aggct	taa	agaag	jaaa	acad	catto	aaa (	cttaa	aaatt	•	691
gtto	2																695

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WO 2005/014828 104/291 Val Arg Ser Ile Leu His Pro Lys Pro Gln Lys Lys Lys Ser Cys 190 185 180 588 aat att atg taa Asn Ile Met 195 <210> 130 <211> 195 <212> PRT <213> Caenorhabditis elegans <400> 130 Met Ser Ser Pro Ser Arg Gln Ile Lys Cys Val Val Val Gly Asp Gly 10 Thr Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Thr Asp Ser Phe 25 20 Pro Val Gln Tyr Val Pro Thr Val Phe Asp Asn"Tyr Ser Ala Gln Met Ser Leu Asp Gly Asn Val Val Asn Leu Gly Leu Trp Asp Thr Ala Gly 55 Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp 70 75 Val Phe Ile Leu Cys Phe Ser Val Val Ser Pro Val Ser Phe Asp Asn 90 85 Val Ala Ser Lys Trp Ile Pro Glu Ile Arg Gln His Cys Pro Asp Ala 110 105 100 Pro Val Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Glu Ala Glu 120 125 Pro Met Arg Ala Leu Gln Ala Glu Gly Lys Ser Pro Ile Ser Lys Thr 140 135 Gln Gly Met Lys Met Ala Gln Lys Ile Lys Ala Val Lys Tyr Leu Glu 155 150 Cys Ser Ala Leu Thr Gln Gln Gly Leu Thr Gln Val Phe Glu Asp Ala 175 170 165 Val Arg Ser Ile Leu His Pro Lys Pro Gln Lys Lys Lys Lys Ser Cys 190 185 Asn Ile Met 195 <210> 131 <211> 843 <212> DNA <213> Arabidopsis thaliana (mouse-ear cress) <220> <221> CDS <222> (90)..(683) <400> 131 acgcgtcgag aaactccaat tccaaaggct aaatctttga gatcttttt tttataaatt 113 tetetgaaat taataaaett tgaggggaa atg age get teg agg tte gta aag Met Ser Ala Ser Arg Phe Val Lys tgc gtg acg gtt ggt gat gga gct gtc gga aaa act tgt ttg ttg att 161 Cys Val Thr Val Gly Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile 15 tot tac aca ago aac act ttc cot acg gat tat gtg cot acc gtt ttc 209 Ser Tyr Thr Ser Asn Thr Phe Pro Thr Asp Tyr Val Pro Thr Val Phe 35 30 gat aat ttc agt gcc aat gtt gtg gtt aat gga agc act gtg aat ctt 257 Asp Asn Phe Ser Ala Asn Val Val Val Asn Gly Ser Thr Val Asn Leu 50 45 305

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					gca Ala											35	5.
					gaa Glu											40	):
					ggt Gly 110											44	ł:
_		_	_	_	aaa Lys					_	_				- ,	49	€.
_				_	cag Gln				_		_				_	54 ·.	Ł!
					tgc Cys								Val			59	}:
		_	_	_	atc Ile	_			_	_	_		_	_	_	64	Ŧ:
	_	_	_		gcg Ala 190	_	_	_	_		_		_	tgati	tgg	69	}(
aaat	tetet	gt t	ttta	atgta	at tt	ggtt	tttgg	tat	tatta	aatc	ttai	tatca	aat q	gaat	gaatta	75	5 (
atgi	tgtta	aat g	gaca	agaca	ac co	caagt	tttga	a cto	ggtc	ettt	ttgi	ttcti	taa 1	tatta	aatgga	81	L (
atti	tata	aga a	aaaa	aaaaa	aa aa	aaaa	aaaaa	a aaa	a				٠.			84	1:

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195

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Val Thr Val Gly Asp Gly Ala Val Gly Lys Thr Cys Met Leu Ile Ser
                                                                             102
                                            20
                       15
 10
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Tyr Thr Ser Asn Thr Phe Pro Thr Asp Tyr Val Pro Thr Val Phe Asp
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Asn Phe Ser Ala Asn Val Val Val Asp Gly Ser Thr Val Asn Leu Gly
                                                                             198
                                    50
                                                                             246
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 Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu
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                                                     70
          60
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                                                                             294
  Ser Tyr Arg Gly Ala Asp Val Phe Leu Leu Ala Phe Ser Leu Ile Ser
                                                 85
                           80
  aag gcc agt tac gag aat att cac aaa aag tgg ctt ccg gag ctg aaa
                                                                             342
  Lys Ala Ser Tyr Glu Asn Ile His Lys Lys Trp Leu Pro Glu Leu Lys
                                             100
                       95
  90
  cat tat gct cct ggc atc ccc att gtg ctc gtc gga aca aaa tta gat
                                                                             390
  His Tyr Ala Pro Gly Ile Pro Ile Val Leu Val Gly Thr Lys Leu Asp
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                                        115
  ttg agg gat gac aag cag ttc ttg aag gat cat cca gga gca gct tct
                                                                             438
  Leu Arg Asp Asp Lys Gln Phe Leu Lys Asp His Pro Gly Ala Ala Ser
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                                    130
               125
                                                                             486
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  Ile Thr Thr Ala Gln Gly Glu Glu Leu Arg Lys Met Ile Gly Ala Val
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  agg tac tta gag tgc agc tcc aaa acc caa cag aat gtg aag gca gtg
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  Arg Tyr Leu Glu Cys Ser Ser Lys Thr Gln Gln Asn Val Lys Ala Val
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  ttt gat aca gcg ata agg gta gct ttg agg cca cca aag gca aag aaa
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  Phe Asp Thr Ala Ile Arg Val Ala Leu Arg Pro Pro Lys Ala Lys Lys
                                                                   185
                                             180
                       175
  aag ata aaa cca ttg aag act aag aga tca aga ata tgc ttt ttc cta
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  Lys Ile Lys Pro Leu Lys Thr Lys Arg Ser Arg Ile Cys Phe Phe Leu
                                         195
                   190
  taatatctga acagatttca ataaataaca aacatttata tatacttgta ttttgatatt
                                                                              690
  tttttgaata ttttctactt gaaatagtgg actttgcttc atcacgttat tggcgagagt
                                                                              750
  attgtcgaat catgttacca ttattcggga gaaatttgta aaatagtagt aatttggcaa
                                                                              810
                                                                              841
  gaaaattgag gattgatatt ttttccccat a
```

<sup>&</sup>lt;210> 134

<sup>&</sup>lt;211> 201

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Arabidopsis thaliana (mouse-ear cress)

<400> 134 Met Ser Thr Ala Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val 40 Val Asp Gly Ser Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val Phe Leu Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Ile 90 His Lys Lys Trp Leu Pro Glu Leu Lys His Tyr Ala Pro Gly Ile Pro 100 Ile Val Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe 120 Leu Lys Asp His Pro Gly Ala Ala Ser Ile Thr Thr Ala Gln Gly Glu 135 140 Glu Leu Arg Lys Met Ile Gly Ala Val Arg Tyr Leu Glu Cys Ser Ser Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Thr Ala Ile Arg Val 170 165 Ala Leu Arg Pro Pro Lys Ala Lys Lys Ile Lys Pro Leu Lys Thr 185 Lys Arg Ser Arg Ile Cys Phe Phe Leu 195 <210> 135 <211> 784 <212> DNA <213> Arabidopsis thaliana (mouse-ear cress) <220> <221> CDS <222> (1)..(591) <400> 135 atg agt gct tcg agg ttt ata aag tgt gtc acc gtc ggc gat ggt gcc 48 Met Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala 10 gtc gga aaa act tgt atg ctg att tct tac aca agc aac act ttc cct 96 Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro acg gac tat gtt cca act gtt ttc gac aac ttc agt gct aat gtg gtt 144 Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val gta gat ggg aac acg gtg aat ctt gga ttg tgg gat aca gct ggt caa Val Asp Gly Asn Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln 192 55 60 gaa gac tat aac agg tta aga ccg ttg agt tac cgt ggt gcc gat gtc 240 Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val 70 288 ttc att ctt gca ttc tcg ctt att agc aaa gct agc tac gag aat gta Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val 336 gcc aag aag tgg att cct gag ctt agg cat tat gcc cct ggt gtt cct Ala Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro 105 ata atc ctc gtt gga acg aaa ctc gat ctt cga gat gac aag caa ttc 384 Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe 120 125 tte ata gae cat cet ggt gea gtg cet att act aca aac cag gga gag 432 Phe Ile Asp His Pro Gly Ala Val Pro Ile Thr Thr Asn Gln Gly Glu 135 gaa cta aag aaa ctg ata gga tca cca atc tac att gaa tgt agt tca 480 Glu Leu Lys Lys Leu Ile Gly Ser Pro Ile Tyr Ile Glu Cys Ser Ser 150 155 145 160

170

528

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Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val

165 170 175	
gtg ctt cag cca ccg aaa cag aag aag aag aaa aag aac aag aac cgc Val Leu Gln Pro Pro Lys Gln Lys Lys Lys Lys Lys Asn Lys Asn Arg 180 185	576
tgc gtg ttc ttg tgatcgaaca tctcttaaaa cgaaaaaagg tttaggtaac Cys Val Phe Leu 195	628
aaaagaagct gaaggaaaac gaacacctgc aacattgtat agttgttgaa tccggcttgt	688
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Val Asp Gly Asn Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln 50 55 60	
Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val	
Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val 85 90 95	
Ala Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro  100 105 110 100 100 100 100 100 100 10	
Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe  115  120  125	
Phe Ile Asp His Pro Gly Ala Val Pro Ile Thr Thr Asn Gln Gly Glu 130 135 140 Glu Leu Lys Lys Leu Ile Gly Ser Pro Ile Tyr Ile Glu Cys Ser Ser	
145 150 155 160	
Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val 165 170 175 Val Leu Gln Pro Pro Lys Gln Lys Lys Lys Lys Asn Lys Asn Arg	
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1 5 10 15.	96

ggt gct gtt ggt aaa acc tgt atg ctc atc tgc tac acc agc aat aaa Gly Ala Val Gly Lys Thr Cys Met Leu Ile Cys Tyr Thr Ser Asn Lys

#### 109/291 25 ttc ccc act gac tac ata cca aca gtt ttt gac aac ttt agt gca aat Phe Pro Thr Asp Tyr Ile Pro Thr Val Phe Asp Asn Phe Ser Ala Asn 144 40 gtt gtt gtt gaa ggc acc act gtc aat ttg ggg ctt tgg gac act gct Val Val Val Glu Gly Thr Thr Val Asn Leu Gly Leu Trp Asp Thr Ala 55 ggg caa gaa gac tat aac aga tta agg cct tta agt tac agg gga gca Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala gat gtt ttc gtc ttg tct ttc tca tta gtc agc cga gct agc tac gag 288 Asp Val Phe Val Leu Ser Phe Ser Leu Val Ser Arg Ala Ser Tyr Glu 90 95 aat gtt ttt aaa aag tgg atc cct gaa ctc caa cac ttt gct cca gga Asn Val Phe Lys Lys Trp Ile Pro Glu Leu Gln His Phe Ala Pro Gly 100 105 110 gtt ccc ctt gtc ctt gtt ggt acc aaa tta gat ctt cgt gaa gat aag 384 Val Pro Leu Val Leu Val Gly Thr Lys Leu Asp Leu Arg Glu Asp Lys 120 125 cat tat ttg gct gat cat cct gga cta tcc cct gta act act gca cag 432 His Tyr Leu Ala Asp His Pro Gly Leu Ser Pro Val Thr Thr Ala Gln 135 140 gga gag gag ttg cgt aag cta att ggt gcg acg tat tac att gag tgt 480 Gly Glu Glu Leu Arg Lys Leu Ile Gly Ala Thr Tyr Tyr Ile Glu Cys 155 150 agt toa aaa act caa cag aat gtg aaa gca gtt ttt gat tot gcg ata Ser Ser Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ser Ala Ile 528 170 165 aag gaa gtg atc aaa cct ctg gtt aaa caa aag gag aag act aag aag 576 Lys Glu Val Ile Lys Pro Leu Val Lys Gln Lys Glu Lys Thr Lys Lys 180 185 aag aag aag caa aag tog aat cac ggc tgt tta toa aat gtt otg tgt 624 Lys Lys Lys Gln Lys Ser Asn His Gly Cys Leu Ser Asn Val Leu Cys 200 195 ggg agg ata gtg act cgg cat tgatgacgat gacccaactc agtctgatga 675 Gly Arg Ile Val Thr Arg His 679 tttt

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								10/29								
				165					170			Asp		175		
-			180					185				Lys	190			
Lys	ГÀЗ		Gln	Lys	Ser	Asn		Gly	Cys	Leu	Ser	Asn 205	Val	Leu	Cys	
Gly	Arg 210	195 Ile	Val	Thr	Arg	His 215	200	•			•	203				
<21:	0> 13 L> 63 2> DN 3> Sa	IA.	romy	/ces	cere	evisi	.ae		•							
	0> 1> CI 2> (]		(630)	) -												
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Met	tca Ser	caa Gln	caa Gln	yal val	ggt	aac Asn	ser	Ile	aga Arg 10	Arg	Lys	ctg Leu	Val	Ile 15	Val	
1 ggt	gat Asp	ggt	gcc Ala	tgt Cys	ggt Gly	aag Lys	aca Thr	tgt Cys	tta	tta Leu	atc Ile	gtc Val	ttt Phe	tcc	aag Lys	96
			20					25				gaa	30			144
Ğİy	Gln	Phe	Pro	Glu	Val	Tyr	Val	Pro	Thr	Val	Phe	G1u 45	Asn	TYE	vaı	
Ala	Asp	gtt Val	Glu	Val	Asp	Gly 55	Arg	лrg	Val	GIU	60	gcg Ala	neu	тър	Азр	192
acc Thr	act	ggt Gly	caa Gln	gaa Glu	Asp	tat Tyr	gat Asp	aga Arg	cta Leu	Arg	cca Pro	ttg Leu	tca Ser	tac Tyr	Pro 80	240
65 ga.c	tcc	aat	atc	qta	70 tta	att	tgt	ttc	tct	75 atc	gat	ctt	cca	gat	tct	288
Asp	Ser	Asn	Val	Val	Leu	Ile	Cys	Phe	Ser	Tie	Asp	Leu	Pro	95	ser	
tta Lev	gag Glu	aat Asn	Val	Gln	gaa Glu	aaa Lys	tgg Trp	att Ile 105	ALA	gaa Glu	gta Val	tta . Leu	cat His 110	Pne	tgt Cys	336
caa Glr	ggt Gly	gtg Val	cca Pro	att	att Ile	ctt Leu	. Val	ggt	tqt	aaa Lys	gto Val	. Asp	ttg Leu	aga	aac Asn	384
		115					120	)				125	)		gtt	
Asp	) Pro	Gln	Thr	Ile	Glu	Gln 135	Lev	ı Arg	l Gin	GIU	140	) GII	L GIII	PIC	, vai	
aca	+0=	can	gag	gga	caa	tet	gta	gca	gac	cag	att	ggo	gca Ala	aco Thi	gga Gly	480
716					150	)				1,55	)				700	
tac	tac	gaa	tgt	tcg	gcc	aag	act	ggt	tat	ggt	gto	aga	gaa Gli	ı gtç	g ttt I Phe	528
				165					170	)				1.7:		
gag	gco	gcc	act	aga	gct	tca	tte	g ato	g ggt	aaa Tws	tci Se:	t aaa r Lvs	a aco	j aai Asi	r ggt n Gly	576
			180	)				185	5				190	,		
aaa	a gct	aag	aag	aac	act	act	gaa	a aag	g aag	g aag	aa Lv	g aag s Lv:	g tgt s Cvs	gt: Va:	c ttg l Leu	f 624 L
гХ	s Alč	1 Lys		a ASI		_ 1111	200	0	- ~ <sub>1</sub> ,	- → <i>I</i> •	- <b>-</b> 7	20	5			
tt: Le	a tag u	3														630

<sup>&</sup>lt;210> 140 <211> 209 <212> PRT

<sup>&</sup>lt;213> Saccharomyces cerevisiae

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Pro Glu Asp Gly Arg Ala Met Ala Glu Lys Ile Asn Ala Tyr Ser Tyr 150 155	
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tgt gtt gta ttg tgaataagtc gctgttttct tcaattcccc acaacagggc Cys Val Val Leu 190	629
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<210> 142 <211> 192 <212> PRT <213> Aplysia californica (California sea hare)

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<210> 143 <211> 579 <212> DNA <213> Homo sapiens (man)

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<210> 144 <211> 192 <212> PRT <213> Homo sapiens (man)

taa

<221> CDS

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Leu Cys Pro Pro Pro Val Lys Lys Arg Lys Arg Lys Cys Leu Leu Leu

140

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                                                                            96
Met Leu Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys Thr Cys
                                   25
cta ctc atg agc tat gcc aac gac gcc ttc ccg gag gag tac gtg ccc
                                                                            144
Leu Leu Met Ser Tyr Ala Asn Asp Ala Phe Pro Glu Glu Tyr Val Pro
                              40
acc gtc ttc gac cac tac gca gtc agc gtc acc gtg ggg ggc aag cag
Thr Val Phe Asp His Tyr Ala Val Ser Val Thr Val Gly Gly Lys Gln
                                                                            192
                                               60
                         55
                                                                            240
tac ctc cta gga ctc tat gac acg gcc gga cag gaa gac tat gac cgt
Tyr Leu Leu Gly Leu Tyr Asp Thr Ala Gly Gln Glu Asp Tyr Asp Arg
                     70
ctg agg cct tta tct tac cca atg acc gat gtc ttc ctt ata tgc ttc
                                                                            288
Leu Arg Pro Leu Ser Tyr Pro Met Thr Asp Val Phe Leu Ile Cys Phe
                                                             95
                                       90
                 85
tcg gtg gta aat cca gcc tca ttt caa aat gtg aaa gag gag tgg gta
                                                                            336
Ser Val Val Asn Pro Ala Ser Phe Gln Asn Val Lys Glu Glu Trp Val
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                                                        110
ccg gaa ctt aag gaa tac gca cca aat gta ccc ttt tta tta ata gga
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Pro Glu Leu Lys Glu Tyr Ala Pro Asn Val Pro Phe Leu Leu Ile Gly
                              120
                                                    125
        115
act cag att gat ctc cga gat gac ccc aaa act tta gca aga ctg aat
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Thr Gln Ile Asp Leu Arg Asp Asp Pro Lys Thr Leu Ala Arg Leu Asn
                          135
                                               140
gat atg aaa gaa aaa cct ata tgt gtg gaa caa gga cag aaa cta gca
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Asp Met Lys Glu Lys Pro Ile Cys Val Glu Gln Gly Gln Lys Leu Ala
                                           155
                      150
aaa gag ata gga gca tgc tgc tat gtg gaa tgt tca gct tta acc cag
                                                                            528
Lys Glu Ile Gly Ala Cys Cys Tyr Val Glu Cys Ser Ala Leu Thr Gln
                                                             175
                                       170
                                                                            576
 aag gga ttg aag act gtt ttt gat gag gct atc ata gcc att tta act
Lys Gly Leu Lys Thr Val Phe Asp Glu Ala Ile Ile Ala Ile Leu Thr
                                   185
             180
 cca aag aaa cac act gta aaa aaa aga ata gga tca aga tgt ata aac
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 Cys Cys Leu Ile Thr
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<sup>&</sup>lt;210> 146

<sup>&</sup>lt;211> 213

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Homo sapiens (man)

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Leu	Leu	Met 35	Ser	Tyr	Ala	Asn	Asp 40	Ala	Phe	Pro	Glu	Glu 45	Tyr	Val	Pro		
Thr	Val 50	Phe	qaA	His	Tyr	Ala 55	Val	Ser	Val	Thr	Val 60	Gly	Gly	Lys	Gln		
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Leu	Arg	Pro	Leu	Ser 85	Tyr	Pro	Met	Thr	Asp 90	Val	Phe	Leu	Ile	Cys 95	Phe		
			100		Ala			105			_		110	_			
		115					120					125			Gly	•	•
	130				Arg	135			_		140	-	. T		•		•
145					Pro 150					155			_		160		
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50	55		60	
Asp Tyr Asp Arg 3	70		75	80
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	165	170		175
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cgc aca gtg aac Arg Thr Val Asn 50	ctg aac ctg Leu Asn Leu 55	g tgg gac act 1 Trp Asp Thr	geg gge cag gag Ala Gly Gln Glu	g gag tat 192 1 Glu Tyr
gac cgc ctc cgt		c tac cct cag		gtc atc 240

240

Asp 65	Arg	ren	Arg	Thr	Leu 70	Ser	Tyr	Pro	Gin	Thr 75	Asn	Val	Phe	Val	80		
Cys	Phe	Ser	Ile	gcc Ala 85	Ser	Pro	Pro	Ser	Tyr 90	Glu	Asn	Val	Arg	His 95	Lys		288
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				aag Lys													384
				agc Ser												. ·	432
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	agc Ser 705	Thr	Gln	Ser	Ala	ctg Leu 710	Ser	aaa Lys	yac Asp	Pro	aac Asn 715	gag Glu	aag Lys	Arg	gat Asp	cac His 720		2160

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725

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Asp Glu Leu Gly Arg Ser Arg Lys Met Ser Lys Asp Gly Lys Lys Lys

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ga Gl	a aa u Ly	g to	g gt	g cc	t ga o Gl	g at u Il	a ac e Th	t ca r Hi	c ca s Hi	ic to	st co s Pi	ca aa co Ly	ag ac	r P	ct tt	.e	1296

								-									
	a++	~++	420	2.at	<b>a</b>			425		~~ +			430	· 			1244
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gag	aaa	ctt	gcc	aag	aac	aaa	cag	aag	cct	atc	act	cca	gag	act	gct		1392
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7nr 545	Leu	гуя	Pne	Ile	550	Thr	ınr	GIY	гÀг	ьеи 555	Pro	vaı	Pro	Trp	Pro 560	*	,
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Tyr Val Pro Thr Val Phe Glu Asn Tyr Thr Ser Lys Ile Thr Arg Asp

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75

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398

446

70

80

# WO 2005/014828 PCT/EP2004/008136

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PLO	Pro	GILL		PLO	GIII	TIIT	wrg		пÄр	пАя	ser	ASII		THE	var		•
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582

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 Cys Phe Ser Val Val Ser Pro Ser Ser Tyr Glu Asn Ile Lys Glu Lys
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Gly	cag Gln	Glu 65	Asp	Tyr	Asp	Arg	Leu 70	Arg	Pro	Leu	ser	75	PIO	Asp	Ser		242
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626

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40 Lys Pro Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr 55 60 50 Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Ile 70 75 Cys Phe Ser Leu Val Ser Pro Ala Ser Phe Glu Asn Val Arg Ala Lys 90 85 Trp Tyr Pro Glu Val Arg His His Cys Pro Asn Thr Pro Ile Ile Leu 110 100 105 Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Asp Thr Ile Glu Arg 125 120 115 Leu Arg Asp Lys Lys Leu Ala Pro Ile Thr Tyr Pro Gln Gly Leu Ala 135 140 Met Ala Arg Glu Ile Gly Ser Val Lys Tyr Leu Glu Cys Ser Ala Leu 150 1.55 Thr Gln Arg Gly Leu Lys Thr Val Phe Asp Glu Ala Ile Arg Ala Val 170 165 Leu Cys Pro Pro Pro Val Lys Lys Pro Gly Lys Lys Cys Thr Val Phe 185 190 <210> 165 <211> 731 <212> DNA <213> Gallus gallus <220> <221> CDS <222> (48)..(638) <400> 165 56 eggecategt cetgetgeac ggcaaggeca gettggegag eetggee atg gee gee Met Ala Ala 104 atc cgc aag aag ctg gtg gtg gtg gga gac ggc gcc tgt ggc aag acc Ile Arg Lys Lys Leu Val Val Val Gly Asp Gly Ala Cys Gly Lys Thr 10 tgc ctc ctc atc gtc ttc agc aag gac gag ttc ccc gag gtt tac gtg 152 Cys Leu Leu Ile Val Phe Ser Lys Asp Glu Phe Pro Glu Val Tyr Val 30 25 20 200 ccc acc gtc ttt gag aac tac gtg gcc gac atc gag gtg gac ggc aag Pro Thr Val Phe Glu Asn Tyr Val Ala Asp Ile Glu Val Asp Gly Lys 45 40 cag gtg gag ctg gcg ctg tgg gac acg gcc ggc cag gag gac tac gac 248 Gln Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asp 60 55 cgc ctg cgc cct ctc tcc tac cca gac acg gac gtg atc ctc atg tgc 296 Arg Leu Arg Pro Leu Ser Tyr Pro Asp Thr Asp Val Ile Leu Met Cys ttc tca gtg gac agc ccg gac tcg ctg gag aac atc ccg gag aag tgg 344 Phe Ser Val Asp Ser Pro Asp Ser Leu Glu Asn Ile Pro Glu Lys Trp 95 90 gtg ccc gaa gtc aag cac ttc tgc ccc aac gtc ccc atc atc ctg gtg 392 Val Pro Glu Val Lys His Phe Cys Pro Asn Val Pro Ile Ile Leu Val 105 110 100 gec aac aag aaa gac etg ege aac gac gag cac gtg egt aac gag etg 440 Ala Asn Lys Lys Asp Leu Arg Asn Asp Glu His Val Arg Asn Glu Leu 125 120 gcc cgc atg aag cag gag ccg gtg cgc act gag gat ggc cgc gcc atg 488 Ala Arg Met Lys Gln Glu Pro Val Arg Thr Glu Asp Gly Arg Ala Met 140 135 gcc atc cgc atc cag gcc tac gac tac ctg gag tgc tcg gcc aag acc 536 Ala Ile Arg Ile Gln Ala Tyr Asp Tyr Leu Glu Cys Ser Ala Lys Thr 1,55 160 aag gag ggt gtg cgg gag gtc ttt gag acg gcc acc cgg gcg gcc ttg 584 Lys Glu Gly Val Arg Glu Val Phe Glu Thr Ala Thr Arg Ala Ala Leu 175 165 170 cag aag cgc tac ggc act cag aac ggc tgc atc aat tgc tgc aag gtc 632 Gln Lys Arg Tyr Gly Thr Gln Asn Gly Cys Ile Asn Cys Cys Lys Val

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Arg 145	130 Ala	Met	Ala	Ile	Arg 150	135 Ile	Gln	Ala	Tyr	Asp	Tyr	Leu	Glu	Cys			•
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					aaa Lys											•	108
ggg			Cys		ctc Leu			Phe	agc				Phe	cct			156
		Val			gtt Val		Glu					Asp					204
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Ser Lys Lys Trp Val Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro
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Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg His Asp Lys Gln Phe
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Phe Ala Glu His Pro Gly Ala Val Pro Ile Ser Thr Ala Gln Gly Glu
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Glu Leu Lys Lys Leu Ile Gly Ala Pro Ala Tyr Ile Glu Cys Ser Ala
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Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val
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                                                                           234
                                Met Ser Ser Gly Arg Pro Ile Lys Cys
 gtg gtg gtc ggc gac ggc acg gtg ggg aag acg tgc atg ttg atc agc
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 Val Val Val Gly Asp Gly Thr Val Gly Lys Thr Cys Met Leu Ile Ser
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Tyr Thr Thr Asp Ser Phe Pro Gly Glu Tyr Val Pro Thr Val Phe Asp
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                                                                           378
 Asn Tyr Ser Ala Pro Met Val Val Asp Gly Val Gln Val Ser Leu Gly
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ccg Pro 90	tcg Ser	tcg Ser	ttc Phe	gaa Glu	aac Asn 95	gtt Val	acc Thr	tcc Ser	aaa Lys	tgg Trp 100	tat Tyr	ccc Pro	gag Glu	atc Ile	aag Lys 105		522
cac His	cac His	tgc Cys	ccg Pro	gat Asp 110	gcg Ala	ccc Pro	atc Ile	att Ile	tta Leu 115	gtc Val	gga Gly	acc Thr	aaa Lys	atc Ile 120	gat Asp		570
											gcg Ala						618
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	gta Val				tag											· .	780

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<213> Anopheles gambiae str

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<220>

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Ile	Lys	Ala	Val	Val	Val	Gly	Asp	Gly	Ser	Val	Gly	Lys	Thr	Cys	Leu		
	_		20			_	_	25					30				
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		35					40				-	45					
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Z-C	Dro	Leg	age cor	Trr	Dro	233	Ala	Wie	Val	Dhe	TAN	T.011	Cvs	Phe	Ser		
ALG	PIO	пеп	per	85	FLO	Gry	ALG	1170	90	FIIC	LCG	u	CyD	95	501		
ata	~++	+ = =	200		tar	+++	gca	220		202	tee	222	taa		aca		336
gre	911	Com	age	mb-	ccg	Dho	Ala	Aac	TIO	Aya Ara	602	Larg	TYP	Tur	Thr		230
var	val	ser		1111	ser	Pire	Ата	105	TT6	ALG	Ser	цуз	110	TYL	T117		
			100		+~+					- t-	ata	art		aaa	202		384.
gag	gte	aag	gag	Tac	cgc	Dea	aac	919	Dwo	Mot	TIO	LOU	7727	99ª	Thr		<b>30</b> 4.
GIU	val		GIU	TAT	Cys	PIO	Asn	vai	PIO	Met	TTE	125	vai	GTA	TIIL		
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aag	tat	gac	ctg	crg	TCC	gac	gag	gct	Tac	ccg	370	aay	acy	T	gag		432
гла		Asp	ьeп	reu	ser		Glu	ALG	TAL	пеп		гуу	Mec	nys	GIU		
	130					135					140						400
aag	aac	caa	tcc	ccg	ara	CCC	gat	gaa	cgt	gca	gag	gaa	get	gca	aaa Tara		480
-	Asn	GIN	ser	PLO		ser	Asp	GIU	Arg		GIU	GIU	val	ALA			
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Glu	Ile	Lys	Ala		Lys	Tyr	Ile	ser		ser	Ala	Arg	Cys	GIN	Leu		
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cgc	gta	aag	gac	gtā	ttt	gat	agt	gca	atc	cgc	aca	gct	CCC	aag	aat		576
Arg	Val	Lys		Val	Phe	Asp	Ser		Ile	Arg	Ala	Ala		гăа	Asn		
			180					185					190				
atg	ggg	atg	atg	ggt	agt	aāa	act	tcc	aag	gca	gga	aag	aaa	aag	gat		624
Met	Gly	Met	Met	Gly	Ser	Gly	Thr	Ser	Lys	Ala	Gly		Lys	Lys	Asp		
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gga	tct	gga.	aag	gga	aag	tgt	gtt	ata	ttc	tag							657
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<212> PRT <213> Giardia lamblia ATCC 50803

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Lys Tyr Asp Leu Leu Ser Asp Glu Ala Tyr Leu Ala Lys Met Lys Glu 135 140 Lys Asn Gln Ser Pro Val Ser Asp Glu Arg Ala Glu Glu Val Ala Lys Glu Ile Lys Ala Ile Lys Tyr Ile Ser Cys Ser Ala Arg Cys Gln Leu . 170 Arg Val Lys Asp Val Phe Asp Ser Ala Ile Arg Ala Ala Leu Lys Asn . 185 Met Gly Met Met Gly Ser Gly Thr Ser Lys Ala Gly Lys Lys Lys Asp 200 Gly Ser Gly Lys Gly Lys Cys Val Ile Phe 215 <210> 175 <211> 624 <212> DNA <213> Neurospora crassa <220> <221> CDS <222> (1)..(624) <400> 175 atg gtg acg gga act atc aag tat gcc aaa aca aac cac ccc tta tcg 48 Met Val Thr Gly Thr Ile Lys Tyr Ala Lys Thr Asn His Pro Leu Ser 10 aga gag tgc gta gtc gtc ggt gac ggt gcc gtt gga aag aca tgt ctc 96 Arg Glu Cys Val Val Val Gly Asp Gly Ala Val Gly Lys Thr Cys Leu 20 25 ctc atc agc tat aca acg aat aag ttc ccc tcg gaa tat gtg ccg aca 144 Leu Ile Ser Tyr Thr Thr Asn Lys Phe Pro Ser Glu Tyr Val Pro Thr 40 45 gtt ttc gac aac tat gcc gtc acc gtc atg atc ggt gat gag ccc tat 192 Val Phe Asp Asn Tyr Ala Val Thr Val Met Ile Gly Asp Glu Pro Tyr 55 acg ctc ggc ctg ttc gat aca gca gga caa gaa gat tac gac cgt tta 240 Thr Leu Gly Leu Phe Asp Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu 70 75 cgt ccg cta tca tac ccc cag acc gac gtc ttc ctc atc tgc ttc agc Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Ile Cys Phe Ser 288 85 90 gtt gca tcg ccc gcc tcg ttc gaa aac gtg tcc cag aaa tgg gcc ccc 336 Val Ala Ser Pro Ala Ser Phe Glu Asn Val Ser Gln Lys Trp Ala Pro 110 100 105 gaa gtc aac cat cac tgc ccc ggc gtg ccc ttc ctc atc gtc gga acg Glu Val Asn His His Cys Pro Gly Val Pro Phe Leu Ile Val Gly Thr 384 120 cag aag gat ttg cgc tcc gac aag gaa ctg agg gac aag ctt gcc cag 432 Gln Lys Asp Leu Arg Ser Asp Lys Glu Leu Arg Asp Lys Leu Ala Gln 130 135 140 cgc aag cag tcg atg ata gag ttc aag cag gga gag aag ctt gct cag 480 Arg Lys Gln Ser Met Ile Glu Phe Lys Gln Gly Glu Lys Leu Ala Gln 155 150 gat ett gac gec gtc aaa tac gtc gag tgc agt geg etg aca cag gaa 528 Asp Leu Asp Ala Val Lys Tyr Val Glu Cys Ser Ala Leu Thr Gln Glu 170 ggt ctc aag aac gtg ttt gac gag gcc atc gtt gcg gca ctg gag ccg Gly Leu Lys Asn Val Phe Asp Glu Ala Ile Val Ala Ala Leu Glu Pro 576 185 cct cag aaa aag aca agt aaa agg gac aag aag tgc ttg att ctg 621 Pro Gln Lys Lys Thr Ser Lys Arg Asp Lys Lys Cys Leu Ile Leu

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624

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<213> Neurospora crassa

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Arg Lys Gln Ser Met Ile Glu Phe Lys Gln Gly Glu Lys Leu Ala Gln
145 150 155 160
Asp Leu Asp Ala Val Lys Tyr Val Glu Cys Ser Ala Leu Thr Gln Glu
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Pro Gln Lys Lys Thr Ser Lys Arg Asp Lys Lys Cys Leu Ile Leu 195 200 205

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<211> 603

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<213> Neurospora crassa

<220>

<221> CDS

<222> (1)..(603)

<400> 177

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Gly Asp Pro Val Ala Ile Glu Glu Met Arg Lys Arg Ser Gln Arg Phe

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	Met	Glu	Asp	Glu		Gln	Arg	Ile	Ala			Ile	Gly	Ala			•
145	tat	ata	~~~	+~+	150	200	a++	200	~~~	155					160		-
Lvs	Tvr	Leu	Glu	tgt Cys	Ser	Ser	Len	Thr	gga	Glu	ggt	Val	gac	gac	y La		528
-1-	-2-			165		501			170	GIG	O.L.y	Val	Yen	175			
ttc	gag	gca	gcc	acg		gcg	gcg	ctq		acq	ttt	qaq	aaq				576
Phe	Glu	Āla	Ala	Thr	Arg	Ala	Ala	Leu	Leu	Thr	Phe	Glu	Lys	Lys	Glu		
			180	•				185		•			190	_			
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GTÅ	ser		Cys	Cys	Val	ITE									•		
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	Gly	Asp	Gly	Ala	Cvs	Gly	Lys	Thr		Leu	Leu	Ser	Val		Thr		
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Leu	Gly	Phe	Phe	Pro	Ala	Thr	Tyr	Ile	Pro	Thr	Val	Phe	Glu	Asn	Tyr		•
	1	35		_		_	40	_	_	·		45					
Val		Asp	Cys	Arg	Val	Asp	Gly	Lys	Ser	Val		Leu	Ala	Leu	$\mathtt{Trp}$		
7 cn	50 Th~	הוג	Clar	GIn	ai.	25	m.	C1.,	7	Ton	60 3~~~	77.00	¥	77-	(Th. 200		
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	Lys	Ala	His	Val		Leu	Ile	Glv	Phe		Val	Asp	Thr	Pro			
	•			85				4	90					95	F		
Ser	Leu	Asp	Asn	Val	Lys	His	Lys	Trp	Val	Thr	Glu	Ala	Asn	Glu	Arg		
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Сув	Pro		Val	Pro	Ile	Ile		Val	Gly	Leu	Lys	_	qeA	Leu	Arg		
Glar.	7 ~~	115 D~o	77-1	77-	T10	~1··	120	Mode	3	T	7	125	<b>~</b> 1	B	Db -		
	130	PIO	Val	Ala	тте	135	GIU	Mec	Arg	гуя	140	ser	GIN	Arg	Pne		
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Lys	Tyr	Leu	Glu	Cys	Ser	Ser	Leu	Thr	Gly	Glu	Gly	Val	Asp	Asp	Val		
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Phe	Glu	Ala		Thr	Arg	Ala	Ala		Leu	Thr	Phe	Glu		Lys	Glu		
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GTÅ	Ser	195	Cys	Cys	val	TTE	200.										
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	'> .> CD	s															
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	.,-	, - • \	<b> ,</b>														
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LLY Len	Len	61 12 990	yat Aen	ggt Gly	ycc Ma	Cyre	gga	Tara	aCC Th∽	se-	CEG	Len	aaC Aer	ycc Val	Dhe		96
		y	20 20	y	ma.	-ys	-TA	цуя 25	****	n-cT	Ten	-cu	30	v 04.4.	* ***		
aca	aga	ggc		ttc	ccc	act	gta		gaq	ccq	aca	gtc		gag	aac		144
				Phe													<del></del>
•		35					40	-				45					
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	Val 50					55					60					
	gat Asp															240
	gat Asp															288
	tcg Ser															336
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cgc Arg	gag Glu 130	gcg Ala	acc Thr	gag Glu	gac Asp	gaa Glu 135	gag Glu	gat Asp	ggc Gly	gga Gly	gcc Ala 140	aac Asn	gag Glu	gac Asp	ggt Gly	432
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	aac Asn															576
ttg Leu	tca Ser	gtg Val 195	aag Lys	aag Lys	gac Asp	cgg Arg	gag Glu 200	gag Glu	tcg Ser	aag Lys	tgc Cys	gtg Val 205	gtc Val	atg Met		621
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WO 2005/014828

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Val Met Leu Lys Cys Val Val Gly Asp Gly Ala Val Gly Lys Thr
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                                    25
                                                          30
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Cys Leu Leu Met Ser Tyr Ala Asn Asp Ala Phe Pro Glu Glu Tyr Val
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                                                      45
ecc acc gtc ttc gac cac tac gca gtc agc gtt acc gtg gag ggc aag
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Pro Thr Val Phe Asp His Tyr Ala Val Ser Val Thr Val Glu Gly Lys
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cag tac ctg ctg ggg ctc tac gac acc gcc ggg cag gaa gac tat gac Gln Tyr Leu Leu Gly Leu Tyr Asp Thr Ala Gly Gln Glu Asp Tyr Asp
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cgt ctg aga cct tta tct tat cct atg acc gat gtc ttc ctt atc tgc
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Arg Leu Arg Pro Leu Ser Tyr Pro Met Thr Asp Val Phe Leu Ile Cys
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                                        90
ttc tca gtg gta aac cct gct tca ttt caa aac gtg aag gaa gaa tgg
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Phe Ser Val Val Asn Pro Ala Ser Phe Gln Asn Val Lys Glu Glu Trp
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gta ccg gag ttg aag gaa tat gca cct aat gtt cct ttt tta cta gta
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Val Pro Glu Leu Lys Glu Tyr Ala Pro Asn Val Pro Phe Leu Leu Val
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gga aca cag att gat ctt cgt gat gac ccc aaa act ctg gca aga ttg
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Gly Thr Gln Ile Asp Leu Arg Asp Asp Pro Lys Thr Leu Ala Arg Leu
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Asn Asp Met Lys Glu Lys Pro Leu Ser Val Glu Gln Gly Gln Lys Leu
145
                      150
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Ala Lys Glu Ile Gly Ala Tyr Cys Tyr Val Glu Cys Ser Ala Leu Thr
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                                        170
cag aaa gga ctg aag act gtt ttt gat gaa gct att ata gcc att cta
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Gln Lys Gly Leu Lys Thr Val Phe Asp Glu Ala Ile Ile Ala Ile Leu
             180
                                    185
act cca aag aaa cac acg gtg aag aag aga ata ggt tcg aga tgc ata
Thr Pro Lys Lys His Thr Val Lys Lys Arg Ile Gly Ser Arg Cys Ile
                                                                              624
        195
                               200
aac tgc tgt ttg atc acg tga
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Asn Cys Cys Leu Ile Thr
    210
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<212> PRT
<213> Gallus gallus
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Leu

								1.	44/29	1								
	65					70					75					80		
	Arg			Pro.	85					90					95			
				Val 100					105					110				
			115	Leu				120				•	125					
		130		Ile			135					140						
	145			Lys		150					155					160		
				Ile	165					170					175			
				Leu 180					185					190				
			195	Lys			Val	Lys 200	Lys	Arg	Ile	Gly	Ser 205	Arg	Cys	Ile		
• •	Asn	Cys 210	Cys	Lėu"	Ilë	Thr												
		)> 18 L> 58																
	<212	2 > Di	IA.	ydani	lo re	erio												
	<220			•												•		•
		1> CI 2> (:		(582)														
	ato	0> 10 qct	σca	att	cga	aag	aaa	ctt	gtc	ata	gtc	ggt	gat	gga	gcc	tgt	48	}
	Met 1	Āla	Ala	Ile	Arg 5	Lys	Lys	Leu	Val	Ile 10	Val	Gly	Asp	Gly	Ala 15	Сув		:
	ĞÌу	Lys	Thr	tgt Cys 20	Leu	Leu	Ile	Val	Phe 25	Ser	Lys	Asp	Gln	Phe	Pro	Glu	96	
	gtc Val	tac Tyr	gtg Val 35	ccg Pro	aca .Thr	gtc Val	ttc Phe	gag Glu 40	aac Asn	tac Tyr	gtt Val	gca Ala	gat Asp 45	atc Ile	gag Glu	gtc Val	14	4
	gat Asp	tca Ser 50	aaa	cag Gln	gtt Val	gag Glu	ctt Leu 55	qcc	tta Leu	tgg Trp	gat Asp	act Thr 60	gct Ala	gga Gly	cag Gln	gag Glu	19	2
	Asp	tat	gat Asp	cgg Arg	tta Leu	Arg	CCC	ctc Leu	tcc Ser	tat Tyr	Pro	gac	aca Thr	gat Asp	gtt Val	att Ile 80	24	10
-	65 ctc Leu	atg Met	tgc Cys	ttc Phe	tcc Ser	70 atc Ile	gac Asp	agt Ser	cct	Asp	75 agc Ser	ttg Leu	gaa Glu	aat Asn	тте	cca	28	88
	gaa Glu	aaa Lys	tgg Trp	aca Thr	85 cca Pro	gag Glu	gtg Val	aag Lys	cat His	90 ttc Phe	tgt Cys	ccc	aat Asn	gtt Val	95 ccc Pro	atc Ile	33	36
	atc	cto	ata	100 ggt Gly	aac	aaa	aaq	gat	105 ctc	cgg	aat	gat	gag	110 cac	aca	cga	38	34
			115	i				120	1				125	i		aāa	43	32
	Arg	Glu 130	Leu	Ala	Lys	Met	. Lys 135	Gln	Glu	ı Pro	Val	. Lys 140	Pro	Glu	l GI	r GTÅ	4.6	
	cga Arg 145	Asp	ato Met	gcc Ala	aac Asr	cga Arg 150	Ile	aat Asr	. gcc	Phe	ggt Gly 155	y Tyr	Lev	ı gaşı ı Glu	t Cys	tcg Ser 160	40	80
	acc	aaa	aca Thr	aaa Lys	gat Asp 165	ggc	ato	aga Arg	gaa Glu	gto Val	. Phe	gaa Glu	ato Met	gcc Ala	acc Thi	agg Arg	52	28
	gcg	gcg Ala	cto Lev	ı Gln	gco	aga	aaa J Lys	cgt Arg	g Gly	aaa Lys	aag	g ago s Ser	Gly	Cys	cto	g ctg 1 Leu	5'	76
	tta	taa	L	180	•				185	•				190	,		5	82

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Gly Lys Thr Cys Leu Leu Ile Val Phe Ser Lys Asp Gln Phe Pro Glu
Val Tyr Val Pro Thr Val Phe Glu Asn Tyr Val Ala Asp Ile Glu Val
Asp Ser Lys Gln Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu
Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Thr Asp Val Ile
                     70
Leu Met Cys Phe Ser Ile Asp Ser Pro Asp Ser Leu Glu Asn Ile Pro
                                      90
Glu Lys Trp Thr Pro Glu Val Lys His Phe Cys Pro Asn Val Pro Ile
             100
                                  105
Ile Leu Val Gly Asn Lys Lys Asp Leu Arg Asn Asp Glu His Thr Arg
                              120
Arg Glu Leu Ala Lys Met Lys Gln Glu Pro Val Lys Pro Glu Glu Gly
                         135
                                              140
Arg Asp Met Ala Asn Arg Ile Asn Ala Phe Gly Tyr Leu Glu Cys Ser
                     150
                                          155
Ala Lys Thr Lys Asp Gly Val Arg Glu Val Phe Glu Met Ala Thr Arg
                 165
                                      170
Ala Ala Leu Gln Ala Arg Lys Arg Gly Lys Lys Ser Gly Cys Leu Leu
Leu
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<211> 582
<212> DNA
<213> Brachydanio rerio
<220>
<221> CDS
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                                      10
ggg aag acc tgt cta ctc ata gtg ttc agc aaa gac cag ttt cca gaa
                                                                          96
Gly Lys Thr Cys Leu Leu Ile Val Phe Ser Lys Asp Gln Phe Pro Glu
            20
                                 25
gto tac gtg cot act gtg tto gag aac tac att got gac att gaa gto
                                                                          144
Val Tyr Val Pro Thr Val Phe Glu Asn Tyr Ile Ala Asp Ile Glu Val
                             40
gac agc aaa cag gtg gag ctg gca ttg tgg gac aca gca gga cag gag
                                                                          192
Asp Ser Lys Gln Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu
                         55
gae tat gae egt ete aga eet etg tet tae eea gae aca gat gte ate
                                                                          240
Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Thr Asp Val Ile
                     70
                                          75
ctc atg tgc ttc tcc ata gac agt ccc gac agt tta gag aat atc cca
                                                                          288
Leu Met Cys Phe Ser Ile Asp Ser Pro Asp Ser Leu Glu Asn Ile Pro
                                      90
gaa aag tgg acg ccg gag gta aag cac ttc tgc ccc aac gtt ccc ata
                                                                         336
Glu Lys Trp Thr Pro Glu Val Lys His Phe Cys Pro Asn Val Pro Ile
```

105

atc ctg gtg ggc aat aag aga gat ctg cgt act gat gag aac aca cgg

110

384

The Leu Val Gly Asn Lys Arg Asp Leu Arg Thr Asp Glu Asn Thr Arg 115
Arg Glu Leu Thr Lys Met Lys Gln Glu Pro Val Lys Ile Glu Glu Gly 130  agg gac atg gct aac cgc att agc gcc ttc ggc tac ctg gaa tgc tca Arg Asp Met Ala Asn Arg Ile Ser Ala Phe Gly Tyr Leu Glu Cys Ser 145  gct aag act aag gat ggc gtg agg gaa gtt ttt gaa atg gcc acc aga Ala Lys Thr Lys Asp Gly Val Arg Glu Val Phe Glu Met Ala Thr Arg 165  gcg gcg ctg cag gtt cgc aag agg aag aag agg agc ggg tgc tca ctg Ala Ala Leu Gln Val Arg Lys Arg Lys Lys Arg Ser Gly Cys Ser Leu 180  185  582
Arg Asp Met Ala Asn Arg Ile Ser Ala Phe Gly Tyr Leu Glu Cys Ser         145       150       155       160         gct aag act aag gat ggc gtg agg gaa gtt ttt gaa atg gcc acc aga       528         Ala Lys Thr Lys Asp Gly Val Arg Glu Val Phe Glu Met Ala Thr Arg       165       170       175         gcg gcg ctg cag gtt cgc aag agg aag aag aag agg agc ggg tgc tca ctg       576         Ala Ala Leu Gln Val Arg Lys Arg Lys Lys Arg Ser Gly Cys Ser Leu       180       185       190         ttg tga       582
Ala Lys Thr Lys Asp Gly Val Arg Glu Val Phe Glu Met Ala Thr Arg 165 170 175 gcg gcg ctg cag gtt cgc aag agg aag aag agg agc ggg tgc tca ctg Ala Ala Leu Gln Val Arg Lys Arg Lys Lys Arg Ser Gly Cys Ser Leu 180 185 190 ttg tga
Ala Ala Leu Gln Val Arg Lys Arg Lys Arg Ser Gly Cys Ser Leu 180 185 190 ttg tga
203 034

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<210> 186
<211> 193
<212> PRT
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<213> Brachydanio rerio

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Ala Ala Leu Gln Val Arg Lys Arg Lys Arg Ser Gly Cys Ser Leu 185 190 Leu

<210> 187 <211> 806 <212> DNA <213> Ciona intestinalis

<220> <221> CDS <222> (1)..(750)

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#### 147/291.

									gaa Glu								144
									gag Glu								192
									gcg Ala								240
									gca Ala 90								288
									cag Gln								336
									cac His								384
									gtg Val							•	432
Asn 145	Ser	Met	Thr	Arg	Ser 150	Āla	Ser	Met	gca Ala	Thr 155	Thr	Leu	Thr	Thr	Thr 160		480
									tct Ser 170								528
									cac His								576
									aaa Lys							. •	624
									aca Thr								672
									cgt Arg							٠	720
		tgc Cys							tgat	acgo	etg t	tace	ytaaa	at			767
aaat	tgad	ta t	gtac	rgaaa	it q	ctaa	caaa	a tca	atco	rcq							806

<210> 188

<211> 249

<212> PRT

<213> Ciona intestinalis

<400> 188

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									_								
71-	0	115	Th.~	N cm	T.011	7.20	120	Gln.	<b>175 1</b>	λcn	Co~	125	cor	T1_	Sar		
Ala	130					135					140						
Asn 145					150					155					160		
Gly	Val	Asp	Leu	Thr 165	Glu	Met	Thr	Ser	Ser 170	Thr	Leu	Ser	Val	Asn 175	Ser		
Val	Arg	Ala	Glu 180		Gly	Thr	Asp	Arg 185		Asp	Asp	Gln	Ala 190	Ile	Val		
Thr	Thr	Glu 195		Gly	Glu	Lys	Met 200		Lys	His	Ile	Asn 205		Asn	His		
Phe	Val 210		Cys	Ser	Ala	Lys 215		Gly	Thr	Asn	Ile 220		Gln	Val	Phe		
Lys 225		Ala	Ile	Glu	Cys 230		Ile	Lys	Arg	Glu 235		Lys	Val	Gly	Pro 240		
Lys	Asn	Cys	Cys	Cys 245		Leu	Leu	Leu		233						•	
			•	2.23			-		•				•		•		•
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			inte	estir	nalis	3							•				
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	.> CI !> (1		. (598	3)													
<400	> 18	39			•												
ttga	gtto	cat o	· 1	Met (				aaa t Lys 1				Val (	3ly A				49
gcc	ata	σσа		aco aco	tat	cta	ctt	atc	agc	tac	асσ	-	10 aat	acc	ttt		97
Ala	Val	Gly 15	Lys	Thr	Cys	Leu	Leu 20	Ile	Ser	Tyr	Thr	Ala 25	Asn	Ala	Phe		•
								ttt Phe									145
acg Thr	gtc	aac Asn	aat Asn	cag Gln	caa Gln	att	tgc Cys	tta Leu	agt Ser	Leu	tgg	gat Asp	acc Thr	gct Ala	Gly		193
45 Caa	gag	αat	+++	gac	50 agg	tta	aga	ccg	ctt	55 t.ca	tat	cca	gac	acc	60 gat		241
Gln	Glu	Asp	Phe	Asp 65	Arg	Leu	Arg	Pro	Leu 70	Ser	Tyr	Pro	Asp	Thr	Asp		
								att Ile									289
ata	cac	Cac	80 aaa	taa	tta	ccc	gag	85 tta	спа	gaa	cat	tat	90 cct	aat	ata		337
								Leu									
								ctt Leu									385
2++	110	<b>C</b> 22	a=a	att	taa	115	מפכ	aat	cta	222	120	ata	aca	cca	cra a		433
								Asn									±33
125					130					135	_4.4.				140		401
								att Ile									481
tgt	tct	gct	cta	act	cag	gag	tgt	ctc Leu	agc	caa	gta	ttt	gat	gac	gct		529
_			160				_	165					170				c
		Āla					Ser	cac His				Asn					577
acc	tat	175	aarr	ato	att	taa	180 attt:	aca	tata	atte	tt t	185 actt	acag	t.			625
			Lys			cadi		.ca		3 Y				_			023
gtta		gta	ttaa	catt	ac c	gtga	taca	c ac	acga	gttc	ata	gggt	taa	aaac	gagag	ŗt	685

726

tatattttct ttaaaattag ataaacactc attcccgtca a

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							_		_							
			_		_	-	gaa Glu 95				_		_			342
	_		_				gta Val		_				_	-		390
							aaa Lys									438
	_						ctc Leu	_	_				_			486
_					_	_	gcg Ala			_	_			_	_	534
			_	_	_	_	aat Asn 175	_	_			_	-			582
							caa Gln			taat	cago	cat 1	ttaa	gaati	:t	632
tgag	gttaa	acg (	ctcg	aataa	at to	gttca	agtai	t aca	aact	gtat	acca	aaagt	tcc a	ataa	aataa	692
aaat	taaa	aac t	tata	gacti	tt go	etgta	acaca	a tta	atac	atgt	cgti	tacc	gca 1	tgtg	gtgtag	752
ctta	aaac	gat 1	tgtg	caata	ac ci	tttai	tatta	a aa	ggtt	aatg	ttti	tacag	gtc (	gtga	gtaact	812
ggaa	actc	cct 9	gcgt	a	٠											827

<210> 192

<211> 193

<212> PRT

Ile

<213> Ciona intestinalis

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                                              10
 aaa acc tgt ttg ctg atc agc tac aca act aac gct ttc cct gga gaa
                                                                              98
 Lys Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Ala Phe Pro Gly Glu
                  20
                                        25
                                                              30
 tat att ccc act gtg ttt gat aac tac tct gcc aat gtc atg gta gat
                                                                             146
 Tyr Ile Pro Thr Val Phe Asp Asn Tyr Ser Ala Asn Val Met Val Asp
                                    40
 ggc cgc cct gtc aac ttg gga tta tgg gat aca gca gga cag gag gat
                                                                             194
 Gly Arg Pro Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp
                               55
                                                     60
 tat gac aga etc ega ect etc tec tac eca caa ace gat gtt ttt etc
                                                                             242
 Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu
                           70
                                                 75
 att tgt ttc tct gtg gct tct ccc gct tcc tac gaa aac gtg cgc gca
                                                                             290
 Ile Cys Phe Ser Val Ala Ser Pro Ala Ser Tyr Glu Asn Val Arg Ala
                      85
                                            90
 aag tgg cac ccg gag gtc gca cac cac tgc ccg gaa acg ccc gta ctt
                                                                             338
 Lys Trp His Pro Glu Val Ala His His Cys Pro Glu Thr Pro Val Leu
                                       . 105
 ctc gtg gga aca aaa ctt gat tta cgt gac gat gcg gac act gtg aac
Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Ala Asp Thr Val Asn
                                                                             386
              115
                                   120
 aag cta get gag aaa aag ete tee aee att aet aet ee caa ggt tta
                                                                             434
 Lys Leu Ala Glu Lys Lys Leu Ser Thr Ile Thr Thr Gln Gly Leu
         130
                               135
                                                     140
caa atg gcg aag gaa ctg ggg gcg gtt aaa tac caa gag tgc tct gct Gln Met Ala Lys Glu Leu Gly Ala Val Lys Tyr Gln Glu Cys Ser Ala
                                                                             482
                          150
                                                155
 ctg acg caa aag ggg ctg aaa aat gtt ttc gac gaa gcg att cgg gcg
                                                                             530
 Leu Thr Gln Lys Gly Leu Lys Asn Val Phe Asp Glu Ala Ile Arg Ala
                      165
                                            170
 gtt ctt aac cca aca aga aga gtc gtc cga acg aag aac tgc gaa att
                                                                             578
Val Leu Asn Pro Thr Arg Arg Val Val Arg Thr Lys Asn Cys Glu Ile
                 180
                                        185
cta tgattacatt gacatgtaga gcggcctcga acgtttacaa taatttggaa
                                                                             631
Leu
ttatgttcct atttaataaa tggagttcgg tggctttata tattctctct tatcgtttta
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<210> 194 <211> 192 <212> PRT <213> Ciona intestinalis

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Arg	Pro	35 Val	Asn	Leu	Gly	Leu	40 Trp	Asp	Thr	Ala	Gly	45 Gln	Glu	Asp	Tyr		
	50 Arg	Leu	Arg	Pro		55 Ser	Tyr	Pro	Gln		60 Asp	Val	Phe	Leu			
65 Cys	Phe	Ser	Val		70 Ser	Pro	Ala	Ser		75 Glu	Asn	Val	Arg		Lys 80		
Trp	His	Pro		85 Val	Ala	His	His		90 Pro	Glu	Thr	Pro	Val	95 Leu	Leu		
Val	Gly	Thr 115	Lys	Leu	Asp	Leu	Arg 120	Asp	Asp	Ala	qsA	Thr 125	Val	Asn	Lys		
Leu	Ala 130		Lys	Lys	Leu	Ser		Ile	Thr	Thr	Thr 140		Gly	Leu	Gln		
Met 145		Lys	Glu	Leu	Gly 150		Val	Lys	Tyr	Gln 155		Cys	Ser	Ala	Leu 160		
	Gln	Lys	Gly	Leu 165		Asn	Val	Phe	Asp 170		Ala	Ile	Arg	Ala 175			
Leu	Asn	Pro	Thr 180		Ārģ	Val	Val	Arg 185	-	Ľys	Asn	Cys	Glu 190		Leu		
	)> 19																
<21	L> 57 2> Di	<b>IA</b>	٠	4 3		L											
	3 > Ci	lona	inte	28C1I	lalls	3											
	D> L> CI 2> (1		(579)	<b>)</b>												٠	
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atq	caq	gcg	atc Ile	aag Lys	tgt Cys	gtt Val	gtg Val	gtt Val	Gly	gat Asp	gga Gly	gct Ala	gtt Val	Gly	aaa Lys		48
1				5	200	<b>+</b> 24	3.53	3.00	10	act	++0	cct	gga	15	tat	-	96
Thr	Cys	Leu	Leu 20	Ile	Ser	Tyr	Thr	Thr 25	Asn	Ala	Phe	Pro	Gly 30	Glu	Tyr		50
att Ile	ccc Pro	act Thr	gtg Val	ttt Phe	gat Asp	aac Asn	tac Tyr	tct Ser	gcc Ala	aat Asn	gtc Val	atg Met	gta Val	gat Asp	ggc Gly		144
		35					40	~~+		~~~	~~~	45	~~~	ant-	+20		192
Arg	Pro 50	Val	Asn	Leu	Gly	Leu 55	Trp	Asp	Thr	Ala	Gly 399	Gln	gag Glu	Asp	Tyr		192
gac Asp	aga	ctt Leu	cgg Arg	cct Pro	ctc Leu	tcc Ser	tac Tyr	cca Pro	caa Gln	acg Thr	gac Asp	gtt Val	ttt Phe	ctg Leu	atc Ile		240
65			a+ a	~+~	70		~~~	tas	ttc	75 722	226	ata	CCC	aca	80 880		288
Cys	Phe	Ser	Leu	Val: 85	Ser	Pro	Ala	Ser	· Phe 90	Glu	Asn	Val	cgc Arg	Ala 95	Lys		200
tgg Trp	tat Tyr	cca Pro	gaa Glu	gtc Val	gca Ala	cac His	cac His	tgt Cys	cca Pro	gat Asp	aca Thr	ccg Pro	gtc Val	att Ile	ctc Leu		336
gtg	gga	aca	100 aaa	ctt	gat	tta	cgt	105 gac	gac	cag	gaa	acc	110 atc	caa	aag		384
		115					120					125	Ile				
ctg Leu	aaa Lys 130	gaa Glu	aag Lys	aaa Lys	ctt Leu	gcc Ala 135	Pro	atc Ile	ctc Leu	tac Tyr	cca Pro 140	Gln	GJÀ aaa	Leu	cag Gln		432
Met	gcg Ala	aaa Lys	gaa Glu	gtg Val	Asn	gcc	gta	aag Lys	tac Tyr	ctg Leu 155	Glu	tgc Cys	tcg Ser	gct Ala	ctc Leu 160		480
145 acc Thr	caa	aaa Lys	ggc Gly	Leu	Lys	acc Thr	gtt Val	ttc Phe	Asp	gag	gcg	atc Ile	cgc Arg	Ala	gtc		528
cta	tac	cct	gaq	165 caa		cca	aaq	aaa	170 aag	aag	ccc	tgc	gag	175 ctt	ttg		576
Leu	Cys	Pro	Glu 180	Gln	Lys	Pro	Lys	Lys 185	Lys	Lys	Pro	Cys	Glu 190	Leu	Leū		
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Arg Pro Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr
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Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Ile
Cys Phe Ser Leu Val Ser Pro Ala Ser Phe Glu Asn Val Arg Ala Lys
Trp Tyr Pro Glu Val Ala His His Cys Pro Asp Thr Pro Val Ile Leu
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            100
Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Gln Glu Thr Ile Gln Lys
        115
                             120
                                                 125
Leu Lys Glu Lys Lys Leu Ala Pro Ile Leu Tyr Pro Gln Gly Leu Gln
                        135
                                             140
Met Ala Lys Glu Val Asn Ala Val Lys Tyr Leu Glu Cys Ser Ala Leu
                    150
                                         155
Thr Gln Lys Gly Leu Lys Thr Val Phe Asp Glu Ala Ile Ary Ala Val
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Leu Cys Pro Glu Gln Lys Pro Lys Lys Lys Pro Cys Glu Leu Leu
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Gly Lys Thr Cys Leu Leu Ile Val Phe Ser Lys Asp Gln Phe Pro Glu
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                                25
gtt tac gtc cca act gtt ttt gaa aac tat gtg gct gat att gaa gta
                                                                       144
Val Tyr Val Pro Thr Val Phe Glu Asn Tyr Val Ala Asp Ile Glu Val
gac tot aaa cag gtt gag ott got ttg tgg gat aca got ggt caa gaa
                                                                       192
Asp Ser Lys Gln Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu
gat tac gac agg ctt cgt cca ctt tcc tac ccc gat act gat gtt att
                                                                       240
Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Thr Asp Val Ile
                                        75
ctt atg tgt ttc tca atc gac agc cca gat tca ctt gag aac att ccc
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Leu Met Cys Phe Ser Ile Asp Ser Pro Asp Ser Leu Glu Asn Ile Pro
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                                    90
gaa aaa tgg acc cct gag gta agg cat ttt tgc cca agt gtt cca atc
                                                                       336
Glu Lys Trp Thr Pro Glu Val Arg His Phe Cys Pro Ser Val Pro Ile
                                105
att ttg gtt gga aac aaa aaa gat ctt cgt aac gac agt tca aca ata
                                                                       384
Ile Leu Val Gly Asn Lys Lys Asp Leu Arg Asn Asp Ser Ser Thr Ile
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gcg cgc acc aaa gaa ggt gtt cgg gaa gtg ttt gag ctt gca act aaa Ala Arg Thr Lys Glu Gly Val Arg Glu Val Phe Glu Leu Ala Thr Lys 165 170 175	528
gca gct tta caa acc aag aaa aga aag aag agt gga tgt gaa gtc Ala Ala Leu Gln Thr Lys Lys Arg Lys Lys Lys Ser Gly Cys Glu Val 180 185 190	576
ttg taaagaaatt ttaactggag tctagcaatt gacttaacat tggacgcatg Leu	629
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<213> Ciona intestinalis
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30					35					40					Met .		
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Gln	gaa Glu	Asp	Tyr 65	Lys	Lys	Leu	Arg	Pro	Leu	Ser	Tyr	Pro	Gln 75	Thr	Asp		241
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atc Ile	gag Glu 95	acc Thr	atg Met	tgg Trp	atc Ile	aaa Lys 100	gaa Glu	atc Ile	aag Lys	gaa Glu	tac Tyr 105	tgc Cys	cca Pro	gaç Asp	aag Lys		337
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Gln	cgc Arg	Ala	qaA	Glu 130	Leu	Arg	Ala	Lys	Gly 135	Tyr	Glu	Pro	Ile	Pro 140	Arg		433
Ala	rī F	Gly	Glu 145	Glu	Met	Ala	Lys	Lys 150	Ile	Asn	Āla	Cys	Ser 155	Tyr	Ile	• .	481
Glu	tgc Cys	Ser	Ala	Leu	Lys	Ser.	Tyr 165	Asn	Leu	Thr	Glu	Val 170	Phe	Āsp	Glu		529
gcc Ala	gtc Val 175	aag Lys	tac Tyr	gct Ala	ctc Leu	gaa Glu 180	cca Pro	cca Pro	gct Ala	cag Gln	cag Gln 185	acc Thr	cag Gln	act Thr	aaa Lys		577
gaa Glu 190	aag Lys	aca Thr	ggt Gly	ggt Gly	ggc Gly 195	tgc Cys	tgc Cys	gaa Glu	ctt Leu	att Ile 200	taaa	tttt	tt g	rcata	ıtatg	3	630
tac	cagag	jtt a	aaat	aaaa	c at	gttg	raatg	gctg	jtgac	caaa	caac	ttte	ıta a	tccg	ractc	<b>.</b>	690
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gtgtaataat aaaagggaat tagg

<210> 200

<211> 200

<212> PRT

<213> Trichomonas vaginalis

<400> 200

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	130					135					140					
Glu	Glu	Met	Δla	Lvs	Lvs	Ile .	Asn	Ala	Cys	Ser	Tyr	Ile	Glu	Cys	Ser	
1/5					150					155					TOO	
Ala :				165					170					1/3		
Tyr :	Ala	Leu	Glu 180	Pro	Pro .	Ala	Gln	Gln 185	Thr	Gln	Thr	Lys	Glu 190	Lys	Thr.	
Gly	Gly	Gly 195		Суз	Glu	Leu	Ile 200									
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1				5			++~	ata	10	taa	tac	aca	аса		ggg	96
Gly	gct Ala	gtc Val	gga Gly 20	Lys	Thr	Cys	Leu	Leu 25	Ile	Ser	Tyr	Thr	Thr	Asn	Ala	
+++	cct	aac	and a	tac	att	cct	act	atc	ttc	gac	aac	tac	tcg	gcg	agt	144
Phe	Pro	Gly	Glu	Tyr	Ile	Pro	Thr	Val	Phe	Asp	Asn	1yr 45	ser	Ala	ser	
σta	atq	ata	gac	qqa	aag	cct	att	agc	tty	gga	ctg	tgg	gat	act	gcc	192
Val	Met 50	Val	Asp	Gly	Ļys	Pro 55	Ile	Ser	Leu	Gly :	Leu 60	Trp	Asp	Thr	Ala	
aac	<b>727</b>	σaa	gat	tac	qac	aga	ctg	cga	ccg	ctt	tcc	tac	CCC	cag	acc	240
Gly	Gln	Glu	Asp	Tyr	Asp	Arg	Leu	Arg	Pro	ьец 75	ser	TYL	PIO	GIII	80	
C2.C	atc	ttc	ctg	att	tgc	ttc	tcc	atc	gtc	agc	CCC	cca	tcg	ttt	gac	288
Asp	Val	Phe	Leu	Ile	Cys	Phe	Ser	Ile	90	ser	Pro	PIO	Ser	95	Азр	226
aac Asn	gtc Val	aag Lys	gcc Ala	aag Lys	tgg Trp	tac Tyr	ccc Pro	GIU	тте	gat Asp	cat His	cac His	ALA	PIC	aac Asn	336
			1.00					105					T T O			384
atc Ile	Pro	Ile	: Ile	Leu	Val	Gly	Thr	· Lys	Leu	Asp	Leu	Arg 125	GIU	Asp	Pro	
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Asn	130	Lev	ı Glu	Ser	Leu	Arg 135	Gln	. Lys	Arg	Met	140	l Pro	val	. ser	TÄT	
gat	<b>722</b>	ac.c	: ctg	ato	tgc	gcc	aag	gaa	att	aag	gca	cac	aaa	tac	ctg	480
Asp	Gln	Ala	Lev	Ile	Cys	Ala	Lys	Glu	ı Ile	; гла	ATS	l His	Lys	Туг	. neu	
145					150					155	•				100	528
gag	tgt	tct	gcc	: ctg	aca	cag	agg	aat	ctg	aag	ago	gct val	Dhe	. gad	gag	326
				1.65					170	)				T/:		576
gco	: att	: cgt	gct	gto	ctg	aac	CCC	agg	CCC	gto	geg	g cag	Cac	Tag	g aag	576
			180	)				185	g Pro	va.	r Ala	z GII	190	)	s Lys	600
aag	, to	g aag	g tgt	acc	att	ttg	, tga	a								600
Lys	s Sei	Ly:	s Cys	Thr	: Ile	. Let	l									
.01	10~ 1	202														

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<211> 199

<212> PRT

<213> Colletotrichum trifolii

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#### 157/291.

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7(	O 200:	5/014	828					1	50/20	1					101	,		
					1.55			13	58/29	1 170					175			
	gag Glu	gcc Ala	att Ile	Ile	165 gcc Ala	att Ile	ctg Leu	gct Ala	cct	aaq	aaa Lys	ggc Gly	gca Ala	ctg Leu 190	aag Lys	cga Arg		576
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		> 20 Ala	)4 Asn	Gly	Thr 5	Gly	Ser	Ile	Met	Leu 10	Lys	Cys	Val	Val	Val	Gly		
•				20	Gly				25	Leu				30		Asp		
			25					40					45			Val		
		EΛ			Gly Asp		55					60				Thr Met		
	65					70					/5					80 Phe		
					25					90				Туг	Ala	Pro		
			Pro	100 Tyr				·Gly	Thr					Arg	,	Asp		
	Pro			: Ile	Ala	Lys	Leu 135	120 Asn	Asp	Val	Lys	Glu 140	Lys		Ile	val		
	115		Glr			150	Leu	Ala			TDD	)				160		
	Val				165					7.70					<b>1</b> /-			
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	Arg	Leu	195		Arg	Cys	TIE	200	Cys	· Cyl	, 200		205	5				
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	G12 gg5	Ly	s Th	r Cy	c ct	u Lei	ı Il	e Va	1 Pho 25	e se	г цу	s as	b GT	30	e FI	t gag o Glu		96
	gtt Va:	ta L Ty	r Va	c cc l Pr	a ac	t gte r Va	c tt l Ph	t ga e Gl 40	g aa u As	c ta n Ty	c at r Il	t go e Al	c ga a As 45	ът	a ga e Gl	a gtc u Val		144
	Asj	o Gl	у Гу	a ca s Gl	.n Va	l Gl	u Le 55	g gc u Al	a Le	u Tr	p As	ър тг 60	) IT AL	a GI	.y G.	ig gag In Glu	•	192
	As	t ta p Ty	+ ~=	c ag	g ct	u Ar	c cc g Pr	a ct	t tc u Se	t ta r Ty	.c cc r Pr 75	t ga	it ac	t ga ir As	t gt	g att al Ile 80	<u>:</u>	240
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												atg Met			Arg		528
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cta Leu	taa																582

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<210> 206
<211> 193
<212> PRT
<213> Xenopus laevis
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<211> 1092
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<213> Xenopus laevis
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<221> CDS
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gac agt ttg gaa aat atc cct gag aaa tgg acc cca gaa gtg aaa cat Asp Ser Leu Glu Asn Ile Pro Glu Lys Trp Thr Pro Glu Val Lys His	339
ttc tgc ccc aat gtg cca ata atc ctg gtg gga aac aag aag gat ctg Phe Cys Pro Asn Val Pro Ile Ile Leu Val Gly Asn Lys Lys Asp Leu  110 115 120	387
cgg aat gac gag cac acg cgc cgg gag ttg gcc aaa atg aag cag gag Arg Asn Asp Glu His Thr Arg Arg Glu Leu Ala Lys Met Lys Gln Glu 125 130 135	435
cca gta aga gca gag gga agg gac atg gcc aat cga atc agc gcc Pro Val Arg Ala Glu Glu Gly Arg Asp Met Ala Asn Arg Ile Ser Ala  140 140	483
ttt ggc tac ttg gag tgc tct gcc aag acc aag gat ggc gta aga gaa Phe Gly Tyr Leu Glu Cys Ser Ala Lys Thr Lys Asp Gly Val Arg Glu 160 165	531
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480

<213> Xenopus laevis

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<210> 209

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<213> Brachydanio rerio

<220>

<221> CDS

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Arg Asp Met 1	Ala Asn	Arg Il			he G	ly T	yr Me	et Gl	u Cy	ys S 1	er 60	
gcc aaa aca a Ala Lys Thr	aaa gac Lys Asp	aat at	t cgg l Arg	gag g Glu V	rta t	tt q	aa at lu M	tg go et Al	alı		ga rg	528
gcg gcg ctg	165	cac aa	a aaa	aaq a	170 aag a	gc a	ac a	aa tg	rc t	yt c	tg	576
	180		9 017	185				19	0	•		582
Leu					-							
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<211> 193 <212> PRT	-donio r	erio										
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1 Gly Lys Thr	20			Phe 25	Ser 1			3	J			
Val Tyr Val	Pro Thr		4.0				4	ŧ.o			•	
Asp Ser Lys 50		59	5			•	50					
Asp Tyr Asp 65		70				75					-	
Leu Met Cys	25				90				_	, _		:
Glu Lys Trp	100			105				_				ı
Ile Leu Val 115			120	}				123				
Arg Glu Leu 130 Arg Asp Met		7	35				エぞひ					
Arg Asp Met 145 Ala Lys Thr		150				TDD					100	
Ala Lys Thr Ala Ala Leu	16	5			T/0							
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Leu												
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acc tgc ctg Thr Cys Le	g ctc at u Leu Il	c tcc Le Ser	tac ac Tyr Th	ır Tnı	aac	gcc Ala	ttc Phe	ccc Pro	aaa Lys 30	gag Glu	tac Tyr	96
att ccc ac Ile Pro Th	20		aac ta	25 C ago	tee	. caq	atc	agc	ata	gac	aac	144
35	a 200 0	rc aat	cta to	organ	c acc	: aca	aat	cag	gag	gag	tac	192
Arg Thr Va 50	l Ser L	eu Asn	Leu Ti 55	p As	p Thr	Ala	60 60	Gln	Glu	Glı	ı Tyr	

_	-		_	_	_					aac Asn	_					240
										aac Asn						288
										gtg Val						336
										gac Asp						384
		Glu								cag Gln 140						432
	Āla									gag Glu					• .	480
_	_	_			_	_		_	_	gca Ala		_	-			528
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tga															•	576

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<400> 212

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<210> 213

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<212> DNA

<213> Brachydanio rerio

<220>

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			20				tac Tyr	20	act	caa	acc	tat	ata	qac	ggc	144
		35		ctc Leu		ctg Leu	40	~~ ~	200	acc	aat.	cag	gag	qaq	tac	192
	50			acc Thr		55		000	cad	aca	cac	atc	ttc	atc	atc	240
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				85				tgt Cys	cct Pro	aac	σta	cct	ata	ctg		336
		acc	100 aag Lys				cga Arg	gly	- cac	aad	gag	acc	cta	qag	aag Lys	384
ctg Leu	aag Lys	gag Glu	cag	Gly ggg	atg Met	agt Ser	ccg	acc Thr	act Thr	cca Pro	cag Glr	g caa n Glr	Gly	agt Ser	gca Ala	432
ctg Leu	130 gcc Ala		ago Ser	ato	GTZ	ATO		g cga	tat Tyr	cto Lev	gag i Gli	r tac	tcg Sei	g gco	ctt Leu 160	480
145	i				150	)		. ++	aac Asr	gaa Glu	aca	a orti	a a a	a act	gtt Val	528
				169 gco n Ala	5			- 200	- 222	a aaa	a to	t at	g cte	g cti u Le	t	573
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		16	55/291		, ,	
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Leu Tyr Pro A				ys Cys Val		
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				1	5	1.50
aag aaa ctg g Lys Lys Leu V	tg att gtg al Ile Val 10	gga gat g Gly Asp G	gga gct t Sly Ala C 15	ys Gly Lys	Thr Cys Leu 20	162
ctc atc gtc to Leu Ile Val Pl	tc agc aag he Ser Lys	Asp Gln B	Phe Pro A	at gtt tat sp Val Tyr	Val Pro Thr	210
gtg ttt gag at Val Phe Glu A	ac tat gtg	gct gat a	30 atc gaa g [le Glu V	tg gat gga al Asp Gly	35 aaa cag gtg Lys Gln Val	258
40 gag ttg gcc c	tc tgg gac	45 aca gct g	ggt caa g	50 aa gat tat	gat cgc ttg	306
Glu Leu Ala Lo	eu Trp Asp	60	ary Gill G	65 FIGURE	Asp Arg neu	
agg cca ctc to Arg Pro Leu So	cc tat ccg er Tyr Pro 75	gac act g	Asp Val L	tc ttg ata eu Leu Ile 0	tgt ttc tcc Cys Phe Ser 85	354
att ggc aac c	ct gat agc ro Asp Ser	ttt ggg a	aac atc c Asn Ile P	ca cac aaa	tgg ata cca Trp Ile Pro	402
gaa gta aag c Glu Val Lys H	.90 at ttc tgt is Phe Cys	ccc aac g	95 gtg ccc a Val Pro I	tc atc ctg	100 gtc ggg agc Val Gly Ser	450
aag aag gat c	05 tt ggg aat		L10	ta caa cac	115	498
Lys Lys Asp L 120	eu Arg Asn	Asp Leu F	Asn Thr I	le Gln Glu 130	Leu Ala Lys	
agg aaa caa g Arg Lys Gln G 135	ag ccg gtg lu Pro Val	Lys Pro 0	gaa caa g Blu Gln G	gc cga gat ly Arg Asp 145	ttg gcg aac Leu Ala Asn	546
agc att ggc g Ser Ile Gly A	la Phe Glu	tat gtg g	3lu Cys S	ct gca aag er Ala Lys	Thr Lys Asp	594
150 gga gtg aga a Gly Val Arg L	155 ag gtc ttt	gaa aaa a	agc cac c	.60 aa ggc ttg	165 ctc ttg caa	642
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acg aac cgt g Thr Asn Arg V	tg aag aaa al Lys Lys 85	Lys Thr G	ggc tgc t Gly Cys P 190	tt gtc ttt he Val Phe	tgaagtettt	691
—				ta tttacgaa	tg ttattgtgta	751
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ctga	ccac	cc t	acca	tcca.	t at	atga	gctg	agaa	agaa	agc .	tgttg	gagt	ca co	cact	tgagt		1051
gttt	gctc	cc t	aaca	actt	t aa	tcac	catc	ctta	attç	tct	tcgaa	aatg	tc to	ctcc	aggca		1111
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Gly	Lys	Thr	Cys	Leu	Leu	Ile	Val		Ser	Lys	Asp	Gln	Phe 30	Pro	Asp		•
Val	Tyr	Val	20 Pro	Thr	Val	Phe	Glu	25 Asn	Tyr	Val	Ala	qaA	Ile	Glu	Val		
	_	35					40					45	Gly				
Asp	Tyr	Asp	Arg	Leu			Leu	Ser	Tyr	Pro	Asp	Thr	Asp	Val	Leu 80		
65 Leu	Ile	Cvs	Phe	Ser	70 Ile	Gly	Asn	Pro	Asp	75 Ser	Phe	Gly	Asn	Ile			
				85					90					95	Ile		
			100					105	-				110				
Ile	Leu	Val 115	Gly	Ser	ГÀЗ	Lys	Asp 120	Leu	Arg	Asn	Asp	Leu 125	Asn	Thr	IIe		
	130	Leu				135	Glņ				140		Glu				
		Leu	Ala	Asn	Ser 150	Ile	Gly	Ala	Phe	Glu 155	Tyr	Val	Glu	Сув	160		
145 Ala	Lys	Thr	Lys		Gly	Val	Arg	Lys	Val	Phe	Glu	ГÀв	Ser	His	Gln		
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Val	Phe	•										,					
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1				5				•	10				tca	15			96
Thi	. Cys	Let	ı Lev	ı Ile	e Ser	Tyr	Thr	Thr	Asn	Lys	Phe	Pro	Ser 30	Glu	Tyr		
gtg Val	g cca L Pro	Thi	20 a gtg r Val	g ttt L Phe	gac a Asp	aac Asn	. Туг	25 gcg Ala	gtg Val	acc Thi	gtg Val	Met	ato	G17	gga Gly		144
		35					40					45					

								16 // 2:	<b>91</b> .						•	
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	gtt Val															336
	eja aaa		_		_	_	_		_	_			 	_		384
_	gcc Ala 130	_			Gln	_				_	_		 	_	· .	432
_	gcc Ala	_					_	_		_		_	_			480
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	ГÀг	cca Pro 50	atc Ile	Asn	Leu	Gly	Leu 55	Trp	Asp	Thr	Ala	60 Gly	Gln	GIU	Asp	TYT		192
•	Asp	cgt Arg	Leu	Arg	Pro	Leu 70	Ser	Tyr	Pro	Gln	Thr 75	Asp	Val	Pne	ьeu	80 11e		240
	Cys	ttt Phe	Ser	Leu	Ile 85	Ser	Pro	Thr	Ser	Phe 90	Glu	Asn	Val	Arg	95	гåа	•	336
	Trp	ttt Phe	Pro	Glu 100	Val	Ser	His	His	Cys 105	Pro	His	Thr	Pro	110	TTE	ьeи		384
	Val	ggt Gly	Thr	Lys	Leu	Asp	Leu	Arg 120	Glu	Asp	Lys	Glu	125	ITE	GIU	гуя		432
	Leu	aga Arg 130 gca	Asp	Lys	Lys	Leu	Ser	Pro	Ile	Thr	Tyr	140	GIN	GTA	ьeu	Aia		480
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	Thr	Gln	Lys	Gly	Leu 165	Lys	Asn	Val	Phe	170	GIU	Ala	тте	Arg	175	Val		576
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Leu Arg Asp Lys Lys Leu Ser Pro Ile Thr Tyr Pro Gln Gly Leu Ala 140 135 Met Ala Arg Glu Ile Ser Ala Val Lys Tyr Leu Glu Cys Ser Ala Leu 155 150 Thr Gln Lys Gly Leu Lys Asn Val Phe Asp Glu Ala Ile Arg Ala Val 170 Leu Cys Pro Lys Pro Lys Lys Lys Lys Gly Cys Glu Ile Leu 180 185 <210> 221 <211> 558 <212> DNA <213> Schistosoma japonicum <220> <221> CDS <222> (1)..(558) <400> 221 atg caa gcc atc aaa tgt gta gtt atc ggt gat ggt gct gta gga aaa 48 Met Gln Ala Ile Lys Cys Val Val Ile Gly Asp Gly Ala Val Gly Lys 10 aca tgt ttg ctc att agc tac act aca aat gct ttt cct ggt gag tat 96 Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Ala Phe Pro Gly Glu Tyr 25 gtc cca act gtc ttc gat aac tac tct gcc aat gta atg gtt ggt gaa 144 Val Pro Thr Val Phe Asp Asn Tyr Ser Ala Asn Val Met Val Gly Glu 40 aaa cgt gtg aac ctt ggt ttg tgg gat aca gct ggt caa gaa gat tat 192 Lys Arg Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr gat aga tta cgg cca cta tcg tat cca cag act gac gtt ttc ttg gtt 240 Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Val 75 70 tgc ttt tct ttg atc agt cct tca tca ttt gat aac gtt cgt gct aaa 288 Cys Phe Ser Leu Ile Ser Pro Ser Ser Phe Asp Asn Val Arg Ala Lys 90 85 tgg tat cca gaa ata cgc cac ttt tct cca aac aca ccc att att ctt 336 Trp Tyr Pro Glu Ile Arg His Phe Ser Pro Asn Thr Pro Ile Ile Leu 105 100 gtt gga aca aaa ctg gat ctc cgc aac agt tct acc agt cct aaa aac 384 Val Gly Thr Lys Leu Asp Leu Arg Asn Ser Ser Thr Ser Pro Lys Asn 125 120 aac caa cca tca ata tct tat gaa caa ggt tta att atg gca aga gag 432 Asn Gln Pro Ser Ile Ser Tyr Glu Gln Gly Leu Ile Met Ala Arg Glu 140 135 att gga gct cat aag tat cta gaa tgt tca gcg tta act cag gat gga 480 Ile Gly Ala His Lys Tyr Leu Glu Cys Ser Ala Leu Thr Gln Asp Gly 155 150 tta aca gga tgt ttt cga tgc agc tat ccg ggc agt act cat gcc tcc 528 Leu Thr Gly Cys Phe Arg Cys Ser Tyr Pro Gly Ser Thr His Ala Ser 165 558 age teg gaa aaa aaa aca tac ett atg tga Ser Ser Glu Lys Lys Thr Tyr Leu Met 180

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Glu Pro Pro Ala Pro Lys Lys His Arg Asn Cys Leu Ile Leu

tga

573

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Phe Pro Glu Val His His Cys Pro Gly Val Pro Cys Leu Ile Val
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Gly Thr Gln Thr Asp Leu Arg Asp Asp Leu Ser Val Arg Glu Lys Leu
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Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala Val Gly Lys Thr
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Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val Asn Gly Ala
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Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asn
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				ttg Leu														<b>274</b> °.
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	Ile	Leu		gaag												•		810
•			•											•		ggtgta gactgt		930
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Phe Ile Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val	
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Phe Val Asp His Pro Gly Ala Thr Pro Ile Thr Thr Ala Gln Gly Glu	
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Lys Thr Gln Leu Asn Val Lys Gln Val Phe Asp Ala Ala Ile Lys Val	
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		125						-+~	~~~	as a	224		aac	act	tac		485
gtt	agt	aac	gaa	gat	gga	alg	310	Mot	yca NI n	yac Nan	Larg	Tla	Glv	Mla	Tur	_	
Val	Ser	Asn	GIU	Asp	GTA			Mer	ALG	Asp	150	116	GLY	ALG	-7-		
	140					145				~~~		art-	caa	ma a	αtα		533
gga	tat	atg	gaa	tgt	tca	geg	cgc	mb~	T	gaa	995	Val	. Ara	Glii	Val		233
	Tyr	Met	GIU	Cys	ser	Ala	ALG	TIIL	пуэ	165	GTÅ	val	AL 9	014	170		
155					160			++-	~~~		224	222	202	aan			581
ttt	gag	CLL	gca	act	aaa	gca	get	tta	Caa	mb~	Larg	Tara	Ara	Tare	aaa		501
	Glu			175					180					1.85			
aag	agt	qqa	tct	qaa	gtc	ttg	taa	agaa	att	ttaa	ctgg	ag t	ctag	caat	t		632
Lvs	Ser	ĞĬv	Ser	Ğlu	Val	Leu		_									
-2 -		- 4	190														
gac	ttaa	cat	tgga	cgca	tg c	tttc	at										659

<210> 232 <211> 193

<212> PRT

<213> Ciona intestinalis

<400> 232 Met Xaa Ser Ile Arg Lys Lys Leu Lys Ile Asp Gly Glu Gly Ala Cys 10 Gly Lys Thr Cys Leu Leu Ile Xaa Phe Ser Lys Asp Gln Phe Pro Glu 25 20 Val Tyr Val Pro Thr Val Phe Glu Asn Tyr Val Ala Asp Ile Glu Val 40 Asp Ser Lys Gln Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu 60 55 Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Thr Asp Val Ile 75 70 Leu Met Cys Phe Ser Ile Asp Ser Pro Asp Ser Leu Glu Asn Ile Pro 90 85 Glu Lys Trp Thr Pro Glu Val Arg His Phe Cys Pro Ser Val Pro Ile 110 105 100 Ile Leu Val Gly Asn Lys Lys Asp Leu Arg Asn Gly Ser Ser Thr Ile 125 120 115 Lys Glu Leu Ala Lys Met Lys Gln Ser Ala Val Ser Asn Glu Asp Gly 140 135 Met Ala Met Ala Asp Lys Ile Gly Ala Tyr Gly Tyr Met Glu Cys Ser 155 150

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177/291 Ala Arg Thr Lys Glu Gly Val Arg Glu Val Phe Glu Leu Ala Thr Lys 170 Ala Ala Leu Gln Thr Lys Lys Arg Lys Lys Ser Gly Ser Glu Val <210> 233 <211> 567 <212> DNA <213> Schistosoma mansoni <220> <221> CDS <222> (1)..(567) <400> 233 atg caa gcc atc aaa tgt gtg gtt gtc ggt gat ggc gct gtc gga aag Met Gln Ala Ile Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys 10 acc tgt tta ctc att agc tac acg acg aat gcc ttt cct ggt gag tac 96 Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Ala Phe Pro Gly Glu Tyr 20 25 gtc cca acc gtt ttc gat aac tat tct gcc aac gta atg gtt gac cga 144 Val Pro Thr Val Phe Asp Asn Tyr Ser Ala Asn Val Met Val Asp Arg 40 aaa cct gtg aac ctt ggt ttg tgg gat aca gct ggt cag gag gat tat 192 Lys Pro Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr 55 gac aga cta aga cca ctc tca tat cca caa act gat gtg ttt ttg gtg 240 Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Val 70 75: tgc ttc tcc tta gtc agt cgc aca tcg ttc gag aat gtt cgt agt aaa 288 Cys Phe Ser Leu Val Ser Arg Thr Ser Phe Glu Asn Val Arg Ser Lys 85 90 tgg cat ccg gag ata tcc gca tat gtt cca aga gct cct att att ctt 336 Trp His Pro Glu Ile Ser Ala Tyr Val Pro Arg Ala Pro Ile Ile Leu gtc gga act aaa cga gac ctt cgg gat agt cct aat ggc cta aaa tca 384 Val Gly Thr Lys Arg Asp Leu Arg Asp Ser Pro Asn Gly Leu Lys Ser 120 125 aca acg ttt cca gtc acg tat gca gag ggt tgc agg atg gcc aga gaa 432 Thr Thr Phe Pro Val Thr Tyr Ala Glu Gly Cys Arg Met Ala Arg Glu 130 135 140 att aaa get gtg aaa tac etg gaa tge tet get eta aet eag ttt gga 480 Ile Lys Ala Val Lys Tyr Leu Glu Cys Ser Ala Leu Thr Gln Phe Gly 150 155 tta aaa gat gtc ttc gac gaa gct att cga gca gta ctg atg cct gaa 528 Leu Lys Asp Val Phe Asp Glu Ala Ile Arg Ala Val Leu Met Pro Glu 170 ggg aag aaa aag aaa cat agt tca tgt gaa tta att taa 567 Gly Lys Lys Lys His Ser Ser Cys Glu Leu Ile 180 185 <210> 234 <211> 188 <212> PRT <213> Schistosoma mansoni <400> 234 Met Gln Ala Ile Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys 10 Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Ala Phe Pro Gly Glu Tyr 25 Val Pro Thr Val Phe Asp Asn Tyr Ser Ala Asn Val Met Val Asp Arg 40 Lys Pro Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr

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178/291 60 55 Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Val 75 70 Cys Phe Ser Leu Val Ser Arg Thr Ser Phe Glu Asn Val Arg Ser Lys 90 85 Trp His Pro Glu Ile Ser Ala Tyr Val Pro Arg Ala Pro Ile Ile Leu 110 105 100 Val Gly Thr Lys Arg Asp Leu Arg Asp Ser Pro Asn Gly Leu Lys Ser 125 120 Thr Thr Phe Pro Val Thr Tyr Ala Glu Gly Cys Arg Met Ala Arg Glu 140 135 Ile Lys Ala Val Lys Tyr Leu Glu Cys Ser Ala Leu Thr Gln Phe Gly 155 150 Leu Lys Asp Val Phe Asp Glu Ala Ile Arg Ala Val Leu Met Pro Glu 170 165 Gly Lys Lys Lys His Ser Ser Cys Glu Leu Ile 185 180 <210> 235 <211> 600 <212> DNA <213> Penicillium marneffei <220> <221> CDS <222> (1)..(600) <400> 235 atg gcg tct ggg cct gcg act caa tcg ttg aag tgt gtg gtg acc ggt 48 Met Ala Ser Gly Pro Ala Thr Gln Ser Leu Lys Cys Val Val Thr Gly 10 gat ggt gct gtc ggc aag aca tgt ctc ctg ata tca tac acc acc aat 96 Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn 25 20 gec ttt eec gge gaa tac att eec acc gta tte gae aac tac tee get 144 Ala Phe Pro Gly Glu Tyr Ile Pro Thr Val Phe Asp Asn Tyr Ser Ala 40 35 agt gtc atg gtc gac ggc agg ccc atc agc ctc gga ctc tgg gat aca 192 Ser Val Met Val Asp Gly Arg Pro Ile Ser Leu Gly Leu Trp Asp Thr 55 get ggt caa gag gat tat gac egt etc ege eec tta tee tae eet caa 240 Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln 75 70 acc gac gtc ttc ttg atc tgc ttc tct atc gtc tct cca cca tcc ttt 288 Thr Asp Val Phe Leu Ile Cys Phe Ser Ile Val Ser Pro Pro Ser Phe 90 gac aac gta aaa gcc aag tgg ttt ccc gaa atc gag cac cat gca ccc 336 Asp Asn Val Lys Ala Lys Trp Phe Pro Glu Ile Glu His His Ala Pro 105 100 ggc gtg ccc atc att ctt gtc ggc aca aag ctt gat ttg aga gaa gat 384 Gly Val Pro Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Glu Asp 125 120 115 aga gct acc gct gag gcg ctg cga gcc aaa aag atg gag ccg gtg tcg 432 Arg Ala Thr Ala Glu Ala Leu Arg Ala Lys Lys Met Glu Pro Val Ser 135 140 tat gag cag gcg ctt gca gtt gca aag gag att agg gcg cat aag tat Tyr Glu Gln Ala Leu Ala Val Ala Lys Glu Ile Arg Ala His Lys Tyr 480 155 150 145 ctg gag tgt tcg gcc ttg acc cag agg aat ttg aag agc gtg ttt gat 528 Leu Glu Cys Ser Ala Leu Thr Gln Arg Asn Leu Lys Ser Val Phe Asp 170 165 gaa gct att cgg gcc gtc ctc aat cct cgc cct caa ccc aag aac aag 576 Glu Ala Ile Arg Ala Val Leu Asn Pro Arg Pro Gln Pro Lys Asn Lys 180 600 gca aaa cga tgc act att ctg taa

Ala Lys Arg Cys Thr Ile Leu

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<211> 199
<212> PRT
<213> Penicillium marneffei
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Ala Phe Pro Gly Glu Tyr Ile Pro Thr Val Phe Asp Asn Tyr Ser Ala
Ser Val Met Val Asp Gly Arg Pro Ile Ser Leu Gly Leu Trp Asp Thr
Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln
                                         75
Thr Asp Val Phe Leu Ile Cys Phe Ser Ile Val Ser Pro Pro Ser Phe
Asp Asn Val Lys Ala Lys Trp Phe Pro Glu Ile Glu His His Ala Pro
                                105
Gly Val Pro Ile Ile Leu Val Gly Thr Lys Leu Asp Leu Arg Glu Asp
                            120
Arg Ala Thr Ala Glu Ala Leu Arg Ala Lys Lys Met Glu Pro Val Ser
                        135
                                            140
Tyr Glu Gln Ala Leu Ala Val Ala Lys Glu Ile Arg Ala His Lys Tyr
                    150
                                        . 155
Leu Glu Cys Ser Ala Leu Thr Gln Arg Asn Leu Lys Ser Val Phe Asp
                                    170
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Glu Ala Ile Arg Ala Val Leu Asn Pro Arg Pro Gln Pro Lys Asn Lys
            180
                                185
Ala Lys Arg Cys Thr Ile Leu
<210> 237
<211> 845
<212> DNA
<213> Schistosoma japonicum
<220>
<221> CDS
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                                          Met Ser Ala Ile Arg Lys
aag ctc gtt att gtt ggg gat gga gcc tgt ggg aaa act tgt cta cta
                                                                       104
Lys Leu Val Ile Val Gly Asp Gly Ala Cys Gly Lys Thr Cys Leu Leu
                                                     20
            10
ata gta ttt agc aaa gac cag ttt cct gaa gtt tac gtt ccg act gta
                                                                       152
Ile Val Phe Ser Lys Asp Gln Phe Pro Glu Val Tyr Val Pro Thr Val
ttc gaa aac tat gtc gcg gat att gag gta gat aac aaa cag gtt gaa
                                                                       200
Phe Glu Asn Tyr Val Ala Asp Ile Glu Val Asp Asn Lys Gln Val Glu
                                             50
ttg gca ctt tgg gat act gct ggt caa gaa gac tat gac aga tta aga
                                                                       248
Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg
                                         65
                    60
cca ctt tct tac ccc gat acg gat gtt att tta atg tgc ttt agc atc
                                                                       296
Pro Leu Ser Tyr Pro Asp Thr Asp Val Ile Leu Met Cys Phe Ser Ile
                                     80
gac act cca gat agt ttg gaa aac ata cct gag aaa tgg aca cca gaa
                                                                        344
Asp Thr Pro Asp Ser Leu Glu Asn Ile Pro Glu Lys Trp Thr Pro Glu
            90
gtc cga cat ttc tgc cct gat gta cct att gtc tta gtt gga aac aaa
                                                                        392
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Val Arg His Phe Cys Pro Asp Val Pro Ile Val Leu Val Gly Asn Lys

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								100/2	Λ1							
								180/2	91				+	~~~	~~~	440
aaσ	gac	tta	cga	agt	gaa	aac	tca	aca	aga	gat	gac	gga	cat	aga	gga	440
Tvs	Asp	Leu	Arg	Ser	Glu	Asn	Ser	Thr	Arg	Asp	Asp	Gly	His	Arg	GTÅ	
_,_	120		3			125					130					
	120	~~~	+++	att	222	tca	gat	gag	aat.	tat	qca	atq	gcc	gat	cgt	488
aaa -	cag	gaa	Dba	3701	Tira	Cor	) en	G111	GIV	TVY	Δla	Met	Āla	Asp	Arq	
	Gin	GIU	Pne	var		Ser	ASP	GIU	GTY	145				•	150	
135					140								220	ma a		536
att	cat	gct	tac	tca	tat	atc	gag	tgt	tca	gct	aag	acg	aag	gaa	994	550
Ile	His	Ala	Tyr	Ser	Tyr	Ile	Glu	Cys	Ser	Ala	ГÀЗ	Thr	гÀв	Glu	Gry	
				155					160					TPD		
att	cat	gaa	att	ttc	gag	acc	qcg	act	aga	gct	gct	tta	cag	tcg	aag	584
Wal.	720	Glu	Val	Phe	Glu	Thr	Ala	Thr	Arg	Ala	Ala	Leu	Gln	Ser	Lys	
Val	Arg	Gru	170					175					180			
			170			+~+	ant-		att	tga	ttet	caa .	tttt	ctcc	aa	634
aaa	acg	aaa	aag	aay	aay	cyc	3	Tou	TIO	دع د		-55		•		
Lys	Thr	Lys	Lys	гĀз	гÃа	Cys	ASD	nen	Ile							
	•	185					190							~~++	a > a a = +	694
ata	tggti	tat	ccgg	tttt	aa a	gact	tctt	a ca	ttcc	cccc	CCC	cgat	LLC	gett	caggat	034
a++	t	tta.	gact	tttt	at t	aact	actt	a tt	tctt	caac	aaa	cata	ttt	tggt	ttttta	754
all	aaac		9400				_	٠.								
						+	a+++	- ++	atcc	attt	tta	tett	σat.	acta	aaatct	814
aaa	agac	aat	ccat	tcca	tg a	taac	CLLL	a LL	acce	gccc			540			
															•	845
gtc	aggc	ctg	ttaa	aaaa	aa a	aaaa	aaaa	a a								. 043
_		_														

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<210> 239 <211> 582 <212> DNA <213> Ustilago maydis <220> <221> CDS <222> (1)..(582)

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acg tgt o		_				_		_		_			96
atc ccc a Ile Pro T													144
aaa ccc g Lys Pro V 50												•	192
gac cgg t Asp Arg I 65													240
tgc ttt t Cys Phe S													288
tgg tgg c												٠	336
gtg gga a Val Gly 1				g Glu									384
ctg cgc g Leu Arg A													432
atg gcg a Met Ala A 145	agg gac Arg Asp	att cac Ile His 150	gct ac	c aag r Lys	tat Tyr	ttg Leu 155	gag Glu	tgc. Cys	tct Ser	gca Ala	ctc Leu 160		480
acc cag a Thr Gln I	aag gga Lys Gly	ttg aag	ggc gt Gly Va	a ttt l Phe	gat Asp 170	gaa Glu	gcg Ala	atc Ile	agg Arg	agc Ser 175	gtt Val		528
ttg gct o Leu Ala I		cca gtc			aag Lys					ttg			576
ctt taa	100			_00									582

<210> 240 <211> 193 <212> PRT

Leu

<213> Ustilago maydis

<400> 240 Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Ala Phe Pro Gly Glu Tyr 25 Ile Pro Thr Val Phe Asp Asn Tyr Ser Ala Asn Val Met Val Asp Gly 40 Lys Pro Val Ser Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Val Cys Phe Ser Leu Val Ser Pro Pro Ser Phe Glu Asn Val Arg Thr Lys 85 90 Trp Trp Pro Glu Val Ser His His Ala Pro Asn Ile Pro Thr Ile Leu 100 105 Val Gly Thr Lys Leu Asp Leu Arg Glu Asp Pro Glu Thr Ile Ala Lys 120 Leu Arg Asp Arg Met Gln Pro Ile Thr Tyr Ala Gln Gly Asn Gln 135 140 Met Ala Arg Asp Ile His Ala Thr Lys Tyr Leu Glu Cys Ser Ala Leu

155 150 145 Thr Gln Lys Gly Leu Lys Gly Val Phe Asp Glu Ala Ile Arg Ser Val 170 165 Leu Ala Pro Ala Pro Val Gln Ser Lys Lys Lys Asn Asn Cys Leu Ile 190 185 Leu <210> 241 <211> 1196 <212> DNA <213> Ustilago maydis <220> <221> CDS <222> (436)..(1080) <400> 241 aattgcgatg ggatgcaacc gtccacaggg tcccctaagc ccgtgggttc atgtggtcaa 60 cetegecaeg geettgatea acacecaeca cegeattegt agatttteaa acaataeegg 120 ccccatttca tcgccttttg gttttggaag tcaggaacaa gcagcatcat agcaagtgga 180 cgcaccaacg agcccaagtt acagccaatg gacattcagc tttcctccgg ttcgctcgac 240 300 ggccgaatcc tcctctctc tgtcgggaac gggcgcacaa ccattgtagg aattgacacc gattgtttca attgtcccag ccagaagttt gcaccgctca gcacctttgg cattggtagg 360 aacagaaatc ccttttcgtt tccatcgcaa acaggaacac tgtcttgttg atcatctttg 420 ctcccgccgc tcagc atg gca ccg gca gca att tgt agg aag ctt gta att 471 Met Ala Pro Ala Ala Ile Cys Arg Lys Leu Val Ile gtc ggc gac ggt gct tgc ggc aag acg agt ttg ctt tgc gtt ttt gcc 519 Val Gly Asp Gly Ala Cys Gly Lys Thr Ser Leu Leu Cys Val Phe Ala 25 20 567 att ggc gag ttc ccg caa gag tat gaa ccc acc att ttc gaa aac tac Ile Gly Glu Phe Pro Gln Glu Tyr Glu Pro Thr Ile Phe Glu Asn Tyr 30 35 gtc gcc gag atc cgc ctt gat ggc aag cct gtc cag ctg gcg cta tgg 615 Val Ala Glu Ile Arg Leu Asp Gly Lys Pro Val Gln Leu Ala Leu Trp 50 gac acc gcg ggt cag gaa gaa tac gag cgt ctt cgt cca ctc tcc tac 663 Asp Thr Ala Gly Gln Glu Glu Tyr Glu Arg Leu Arg Pro Leu Ser Tyr 75 tca caa gca cac gtc atc ttg atc gcc ttt gcc atc gat aca ccc gac 711 Ser Gln Ala His Val Ile Leu Ile Ala Phe Ala Ile Asp Thr Pro Asp 85 tcg ctc gaa aac gtg caa gtc aag tgg atg gag gta cgt caa ata Ser Leu Glu Asn Val Gln Val Lys Trp Met Glu Glu Val Arg Gln Ile 759 100 105 95 tgc ggc ccc tca gtg cct gtg ctc ctg gta ggc tgc aag aag gat ctt 807 Cys Gly Pro Ser Val Pro Val Leu Leu Val Gly Cys Lys Lys Asp Leu 115 ege gaa aat gee ate get aag gge aag eeg gtt eag ggt eac tat gta 855 Arg Glu Asn Ala Ile Ala Lys Gly Lys Pro Val Gln Gly His Tyr Val 140 135 130 125 aag aga caa cag gct aaa ctg gta gca gca cag atc ggc gct cga tcg 903 Lys Arg Gln Gln Ala Lys Leu Val Ala Ala Gln Ile Gly Ala Arg Ser

		•						103/23	, <b>1</b>					•		٠.	
				145		-			150		•			155			
tat	cac	gaa	tgc	tca	tca	ctc	aac	aac	caa	ggc	gtc	gac	gcc	gtg	ttc		951
Tyr	His	Glu	Cys	Ser	Ser	Leu	Asn	Asn	${\tt Gln}$	Gly	Val	Asp	Ala	Val	Phe		
			160					165					170				
											aat						999
Glu	Ala		Thr	Arg	Ala	Ala	Met	Leu	Val	Arg	Asn	Ser	Gly	Ala	Ser		
		175					180					185					
											gag						1047
Ser	_	Gly	Ala	Ile	Ser		Ser	Lys	Thr	Lys	Glu	Ala	Leu	His	Asn		
	190					195	•				200						
_	_			_		_		_		taga	aato	ctc t	cctto	gtgct	t		1097
_	Ala	Gly	Ser	Cys	Lys	Cys	Ile	Val	Leu			•					
205					210												
cgt	ettgi	ccg a	accci	tgt	cc ta	agco	ctcgc	tct	cgt	etge	cttt	ccat	cg t	cacag	gtaga	t	1157
		-							•							•	
						<b>.</b>			4. 4		•						
CLCC	cctgo	cat t	יבבבנ	gtccc	et co	cacto	CCCC	cat	gtto	cta	*						1196

<210> 242 <211> 214 <212> PRT

<213> Ustilago maydis

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<210> 243 <211> 576 <212> DNA <213> Ustilago maydis <220>

<221> CDS <222> (1)..(576)

210

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Met Gln Thr Ile Lys Cys Val Val Gly Asp Gly Ala Val Gly Lys

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							1	184/29	91							
1				5					10					15		
acc	tgc	ctg	ttg	att	tcg	tac	acc	acc	aac	aag	ttt	CCC	tcg	gag	tat	96
Thr	Cys	Leu	Leu 20	Ile	Ser	Tyr	Thr	Thr 25	Asn	Lys	Pne	Pro	Ser 30	GIu	Tyr	
gtt	ccg	aca	gtg	ttt	gac	aac	tac	gcc	gtg	act	gtc	atg	att	ggc	gag	144
		35					Tyr 40					45				
gat	ccg	tac	aca	ctc	gga	ttg	ttc	gat	acc	gcc	ggt	cag	gag	gac	tac	192
-	50					55	Phe				60					
gac	cga	ctg	cga	ccg	ctt	tca	tac	ccg	cag	acg	gat	gtc	ttc	ctg	gtc	240
65					70		Tyr			75					80	
tgc	ttc	tcg	gtc	acc	tca	cca	gcc	tcg	ttc	gaa	aat	gtc	aag	gaa	aag	288
-				85			Ăla		9.0					95		226
tgg	ttc	ccg	gag	gtg	cat	cac	cat	tgc	cct	ggt	gtg	ccg	tgc	ctg	att	336
_			100				His	105					110			204
gtg	gga	acc	cag	gtg	gat	ttg	cgc	gac	gac	cac	gcc	gtc	atc	gag	aag	384
		115					Arg 120					125				432
ctt	gca	cgt	tca	aag	cag	cgt	cct	gtg	CCC	דדד	gag	gcg	ggt	gag	cgt	434
	130					135	Pro				140					480
ttg	gcg	aga	gag	ttg	ggt	gcg	gtc	aag	tac	gtc	gag	tgc	ccg	315	Len	400
145					150		Val			155					160	528
acg	caa	aag	gga	ttg	aag	aac	gtc	ttc	gac	gag	gcc	atc	grg	gct	gcg	340
				165			Val		170					175		500
ctg	gaa	ccg	cct	gta	atc	cgc	aag	aag	tcc	aag	tgc	gcc	act	CTC		573
Leu	Glu	Pro			Ile	Arg	Lys	Lys	ser	гÀа	cys	Ala	190	теп		
			180					185	1				130			576
tga																

<210> 244 <211> 191 <212> PRT <213> Ustilago maydis

Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys 10 Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Lys Phe Pro Ser Glu Tyr 25 20 Val Pro Thr Val Phe Asp Asn Tyr Ala Val Thr Val Met Ile Gly Glu 40 35 Asp Pro Tyr Thr Leu Gly Leu Phe Asp Thr Ala Gly Gln Glu Asp Tyr 60 55 Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Val 75 Cys Phe Ser Val Thr Ser Pro Ala Ser Phe Glu Asn Val Lys Glu Lys 90 85 Trp Phe Pro Glu Val His His Cys Pro Gly Val Pro Cys Leu Ile 110 105 100 Val Gly Thr Gln Val Asp Leu Arg Asp Asp His Ala Val Ile Glu Lys 125 115 120 Leu Ala Arg Ser Lys Gln Arg Pro Val Pro Phe Glu Ala Gly Glu Arg 135 140 Leu Ala Arg Glu Leu Gly Ala Val Lys Tyr Val Glu Cys Ser Ala Leu 155 150 Thr Gln Lys Gly Leu Lys Asn Val Phe Asp Glu Ala Ile Val Ala Ala 170 Leu Glu Pro Pro Val Ile Arg Lys Lys Ser Lys Cys Ala Ile Leu

190

185/291 180 185

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<210> 246 <211> 210 <212> PRT

<213> Encephalitozoon cuniculi

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170

gct gca tta atg gtt tct aag aag aaa aag tca aag agt ggt gtc tgc

Ala Ala Leu Met Val Ser Lys Lys Lys Ser Lys Ser Gly Val Cys

165

175

PCT/EP2004/008136 **WO** 2005/014828

187/291 180 185 190 aac ctt ttg taa 588 Asn Leu Leu 195 <210> 248 <211> 195 <212> PRT <213> Mucor rouxii <400> 248 Met Ala Glu Ile Arg Arg Lys Leu Val Ile Val Gly Asp Gly Ala Cys Gly Lys Thr Cys Leu Leu Ile Val Phe Ser Lys Gly Thr Phe Pro Glu Phe Tyr Val Pro Thr Val Phe Glu Asn Tyr Val Ala Asp Val Glu Val 40 Asp Gly Lys His Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu 60 Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Ser His Val Ile Leu Ile Cys Phe Ala Val Asp Ser Pro Asp Ser Leu Glu Asn Val Gln 90 Glu Lys Trp Ile Ser Glu Val Leu His Phe Cys Gln Gly Leu Pro Ile 105 Val Leu Val Gly Cys Lys Lys Asp Leu Arg Asn Asp Pro Gly Thr Ile 120 Glu Glu Leu Arg Arg Asn Ser Gln Lys Pro Val Ser Ser Glu Glu Gly 135 140 Ala Ser Ile Ala Gln Arg Ile Ser Ala Tyr Lys Tyr Leu Glu Cys Ser 155 Ala Lys Thr Gly Glu Gly Val Arg Glu Val Phe Glu His Ala Thr Arg 170 165 Ala Ala Leu Met Val Ser Lys Lys Lys Ser Lys Ser Gly Val Cys 185 Asn Leu Leu 195 <210> 249 <211> 1014 <212> DNA <213> Neurospora crassa <220> <221> CDS <222> (259)..(1014) <400> 249 atgregtegt caagcaagtt cegeagetea caccactate attegeagte ggtgtegtea 60 atectaggea ggeacgatag caccagecee ggegeagaac tecaacgaeg accgaecace 120 acctegteet acacateete tggtagegee ageegaegag taccaegega caaegggaeg 180 agatcgagcg atgggacagt gagtaccatg atgagcacca catcgtcgac cggaagagaa 240 tcagcagcaa ctacggcc atg acc gag ggc ccg gcc tac tcc aag aag gtg 291 Met Thr Glu Gly Pro Ala Tyr Ser Lys Lys Val

gtg gtc gtg ggc gat ggc ggt tgc gga aag aca tgt ctc ctg atc agt

Val Val Gly Asp Gly Gly Cys Gly Lys Thr Cys Leu Leu Ile Ser tat agt cag gga tac ttc cca gag aaa tat gtc cca acc gtc ttt gag 339

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Asn	Tyr 45	Ile	Thr	Tyr	Pro	Thr 50	His	Pro	Pro	Thr	ggt Gly 55	Lys	Thr	Val	Glu		435
Leu 60	Ala	Leu	Trp	Asp	Thr 65	Ala	Gly	Gln	Glu	Glu 70	tac Tyr	Asp	Arg	Leu	Arg 75		483
ccg Pro	ctt Leu	tca Ser	tac Tyr	cca Pro 80	gaa Glu	acc Thr	gac Asp	ctt Leu	att. Ile 85	ttt Phe	gtc Val	Cys	ttc Phe	gcc Ala 90	att Ile		531
gac Asp	tgc Cys	ccc Pro	aac Asn 95	tcc Ser	ctc Leu	gag Glu	aat Asn	gtc Val 100	atg Met	gac Asp	aag Lys	tgg Trp	tac Tyr 105	ccc Pro	gaa Glu		579
gtc Val	ctc Leu	cac His 110	ttc Phe	tgt Cys	ccg Pro	tat Tyr	aca Thr 115	ccc Pro	ctt Leu	atc Ile	ctc Leu	gtc Val 120	ggc	ctc Leu	aag Lys		627
töö Ser	gac Asp 125	ctc	cgc Arg	aat Asn	aag Lys	aag Lys 130	acg Thr	tgc Cys	atc Ile	gac Asp	atg Met 135	ctc Leu	aag Lys	aca Thr	caa Gln	*	675
ggt Gly 140	ctc	acc Thr	ccc Pro	gtc Val	acc Thr 145	acc Thr	gaa Glu	caa Gln	gga Gly	ctc Leu 150	gcc Ala	gtc Val	gct Ala	aag Lys	aag Lys 155		723
atq	ggc Gly	gct Ala	cag Gln	tac Tyr 160	atg	gag Glu	tgc Cys	tca Ser	tca Ser 165	aag Lys	gag Glu	atg Met	aag Lys	ggt Gly 170	gta Val		771
gag Glu	gag Glu	att Ile	ttt Phe 175	gag Glu	cag Gln	gcc Ala	atc Ile	ctc Leu 180	aca Thr	gta Val	gtc Val	gcc Ala	aac Asn 185	gac Asp	agg Arg		819
aaa Lys	aca Thr	ctg Leu 190	gaa	cag	gaa Glu	gcc Ala	gcg Ala 195	aac Asn	Gly	atg Met	ctg Leu	ggt Gly 200	gtt Val	ggc	gcg Ala		867
ggc Gly	tcg Ser 205	gga	agc Ser	gga Gly	aag Lys	ggc Gly 210	aqc	gga Gly	atc Ile	tcg Ser	ttc Phe 215	agc Ser	agt Ser	ggt Gly	gac Asp		915
aag Lys 220	gcc	ggt Gly	tcc Ser	Gly 999	ata Ile 225	gly ggg	ccc Pro	gtc Val	aag Lys	gcg Ala 230	gcc Ala	ggt Gly	gtg Val	ggt Gly	ggc Gly 235		963
acq	att Ile	gtc Val	ccg Pro	aaa Lys 240	acg	agg Arg	aag Lys	aag Lys	aag Lys 245	aga Arg	aag Lys	tgt Cys	ggt Gly	atg Met 250	atg Met		1011
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<211> 251

<212> PRT

<213> Neurospora crassa

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Lys	Lys 130	Thr	Cys	Ile	Asp	Met 135	Leu	Lys	Thr	Gln	Gly 140	Leu	Thr	Pro	Val		
Thr 145	Thr	Glu	Gln	Gly	Leu 150	Ala	Val	Ala	Lys	Lys 155	Met	Gly	Ala	Gln	Tyr 160		
	Glu	Cys	Ser	Ser 165		Glu	Met	Lys	Gly 170		Glu	Glu	Ile	Phe 175			
Gln	Ala	Ile	Leu 180		Val	Val	Ala	Asn 185		Arg	Lys	Thr	Leu 190	Glu	Gln		
Glu	Ala	Ala 195		Gly	Met	Leu	Gly 200		Gly.	Ala	Gly	Ser 205		Ser	Gly		•,
Lys	Gly 210		Gly	Ile	Ser	Phe 215		Ser	Gly	Asp	Lys 220		Gly	Ser	Gly		
Ile 225		Pro	Val	Lys	Ala 230		Gly	Val	Gly	Gly 235	Thr	Ile	Val	Pro	Lys 240		
Thr	Arg	Lys	Lys	Lys 245	Arg	Lys	Cys	Gly	Met 250	Met	. ,						
<210	> 25	i1	••		•	-	-		•		.· -				•	•	
	.> 91 !> DN		,	•													
<213	l> 01	yza	sat	iva													
<220	)> .> CI	ns.															
			. (678	3) .													
	> 25										2022						60
ggga	iccai	.ca (	cacc	acco	שני נו	_cacc	acc	ı aa	Juca	acca	ayaa	icaa		LLCag	ggggca		60
aatt	aaga	ag a	igcti	ggt	ga co									aag t			111
:.						1	L.			5	5			Lys (	_		
Val	acc Thr	gtc Val	ggc Gly	gac Asp	ggc	gcc Ala	gtc Val	ggc	aag Lys	Thr	tgc Cys	atg Met	Leu	atc Ile	Ser		159
10 tac	acc	agc	aac	act	15 ttc	ccc	acg	gat	tat	20 gtg	ccg.	acg	gtt	ttc.	25 gac		207
Tyr	Thr	Ser	Asn	Thr	Phe	Pro	Thr	Asp	Tyr 35	Val	Pro	Thr	Val	Phe 40	Asp		
														ctt Leu			255
			45					50	_				55	cct		•	303
		_		_				_				_		Pro			
		aga					ttt					tcc		atc Ile			351
	75		-		= =	80					85			ctg			· 399
Lys	Ala	Ser	Tyr	Glu	Asn 95	Ile	His	Lys	Lys	Trp	Ile	Pro	Glu	Leu	Arg 1:05	٠	
					gtg					gtt				ctt	gac		447
	<u> </u>			110					115		_			Leu 120		•	
			Asp					Leu					Leu	gca Ala			495
att	tcc	act	125 gca	cag	aāa	gag	gag	13 <u>0</u> ctg	aag	agg	atg	ata	135 ggt	gct	gcg		543
		140			_		145	٠.				150		Ala			
														tca Ser		•	591
	155					160	_				165			aag			639
														Lys			
aag					cag Gln					atc		tgag	gtgai	taa			685
-y	USII		y	-y s		9	OGT	-ya	1		u						

170/271		
190 195 acagcaagat tggcgtattc cgcaggaaac ctgtattatt ttt	tacagtgt gtgttgtgtt 745	
atgtttgtgt gttgcagatt agatgcagtt tgggttacaa aat	tttgctgg gtctgaaata 805	
ttcagctcag tgcttcttga gtactacctc tgatgattct tac	caaaagtg ttctttggtt 865	
ggttcagata tatatattat gattattata aaaaaaaaaa	aaaaaaaa 915	
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1 5 10 Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Se	er Asn Thr Phe Pro	
20 25 Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Se	30 er Ala Asn Val Val 45	
35 40 Val Asp Gly Asn Thr Val Asn Leu Gly Leu Trp As 55 60	sp Thr Ala Gly Gln	
Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Ar		
70 75 Phe Leu Leu Ala Phe Ser Leu Ile Ser Lys Ala Se		
His Lys Lys Trp Ile Pro Glu Leu Arg His Tyr Al	la Pro Asn Val Pro 110	
Ile Val Leu Val Gly Thr Lys Leu Asp Leu Arg Gl	lu Asp Lys Gln Phe 125	
Phe Leu Asp His Pro Gly Leu Ala Pro Ile Ser Th	40	
Glu Leu Lys Arg Met Ile Gly Ala Ala Ala Tyr Il	100	
Lys Thr Gln Gln Asn Val Lys Ser Val Phe Asp Se	1/5	
Val Leu Cys Pro Pro Lys Pro Lys Lys Asn Th	hr Arg Lys Gln Arg 190	
Ser Cys Trp Ile Leu 195		
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acg gtc ggc gac ggt gcc gtg ggc aag aca tgt a Thr Val Gly Asp Gly Ala Val Gly Lys Thr Cys M	atg ctc atc tgc tac 157	7
15 . acc agc aac aag ttc ccc act gat tac ata ccc a		5

W O 2003/014828					PC 1/EP2004/000130
-\		19	91/291		
Thr Ser Asr	Lys Phe Pro	Thr Asp :	Tyr Ile Pro	Thr Val Phe .	Asp Asn
ttc agt gca Phe Ser Ala 45	ı aat gtc gtt ı Asn Val Val 50	gtg gat g Val Asp	ggc acc acg Gly Thr Thr 55	gtg aat ttg Val Asn Leu	ggc ctg 253 Gly Leu
tgg gat acc	gca ggg cag		tac aac cga	ctg agg cct Leu Arg Pro	
	gca gat gtt	Phe Val	ctt gca ttc	tca ctt gtg Ser Leu Val 90	agt cga 349
		atg aag a	aag tgg ata	ccg gag ctt Pro Glu Leu 105	
				aca aaa ttt Thr Lys Phe .	
cgt gaa gad Arg Glu Asp 125	aag cac tac Lys His Tyr 130	Leu Met 1	gac cat cct Asp His Pro 135	ggg ttg gtg Gly Leu Val	cct gtt 493 Pro Val 140
acc aca gca Thr Thr Ala	ı caa ggg gag ı Gln Gly Glu 145	gaa ctt o Glu Leu A	cgt aga caa Arg Arg Gln 150	att ggt gct a	atg tat 541 Met Tyr 155
		Lys Thr (		gtc aaa gct Val Lys Ala 170	gtg ttc 589
	lle Lys Val	gta atc	cag cct cca	act aaa cta a Thr Lys Leu 1 185	
aag aag aas	aag aaa tca			atg gtg aac Met Val Asn 200	
tct gga aga	aaa atg cta Lys Met Leu 210	Cys Phe 1		tgatcg aaggg	ggtct 735
	aataccatga g	tgtgacccc	aagttcgcga	agcttgaaat c	ttgatgcgc 795
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								92/29								•	
Asp V				85			•		90					90			
Asn I	le 1	Met	Lys 100	Lys	Trp	Ile	Pro	Glu 105	Leu	Gln	His	Tyr	Ala 110	Arg	Gly		
Val P			Val	Leu	Val	Gly	Thr 120	Lys	Phe	Asp	Leu	Arg	Glu	Asp	Lys		
His T	yr :	115 Leu	Met	Asp	His	Pro 135	Gly	Leu	Val	Pro	Val 140		Thr	Ala	Gln		
Gly G					150	Gln				155	Tyr				TOO		
Ser S	Ser :	ГÀЗ	Thr	Gln 165	Gln	Asn	Val	Lys	Ala 170	Val	Phe	Asp	Ala	Ala 175	Ile		
Lys V			180	Gln				185	Leu				T30	Lys			
Lys S		Arg 195	Lys	Gly	Cys	Ser	Met 200	Val	Asn	Ile	Leu	Ser 205	Gly	Arg	Lys		
Met I			Phe	Lys	Ser			•		<b>-</b> ·				ē		(3)	
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<220			<u>-</u>														
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Thr	Cys	Leu	Leu	Ile	Ser	Tyr	Thr	25	ASD	. тАз	Phe	, PIC	30	. Git	,		A A
gtg Val	ccc Pro	acc Thr	gtc Val	tto Phe	gac Asp	Asr	Tyx	gcc Ala	gtg Val	acc Thr	gto Val	ato Met 45	: Ile	Gly	gag Glu	Τ.	44
gac	ccc	35 tat	aca	ctg	ggt	cte	40 ttt	gat	act	gct	ggo	cag	g gag	g gat 1 Ast	tac Tyr	1	92
	EΛ					55					60					2	40
Asp	cga Arg	Lev	a Arg	g Pro	rttg Leu 70	Sei	Ty:	r Pro	Glr	75	Asj	va.	l Phe	e Le	t gtg 1 Val 80		
65 tgc	ttt	agt	gta	a aca	+ct	cca Pro	gco Ala	c tco	tto r Phe	gag Gli	g aad 1 Asi	e gta n Vai	a aag l Lys	g gaq s Gl	g aaa u Lys	2	88
				85					90					ں و	c atc	3	36
Trp	Phe	Pro	Gl:	ม Vai	L Arc	J Hi:	s Hi	s Cy: 10!	s Pro 5	o GTZ	y va	T Pro	11	0 В ПС	u iie		
gtc Val	ggc Gly	Th	g caa	a atr	c gad a Asp	tte	u Ar	g As	p Ası	c tog o Sei	g ca r Gl	g gt n Va 12		c ga e Gl	g aag u Lys	.3	84
ctg	gcg	11.	~ ~=	a aa	g cag	g ag	12 a cc	a at	c ac	g age	c ga	c ca	a gg	c ga	g cgg	4	132
Leu	Ala	Ar	g G1:	n Ly	s Glı	n Ar 13	g Pr 5	o Va	I Th	r se	14	0 5 GT	II GI	y Gr	u my	,	100
ctc Leu	gtt Val	. cg	g ga g Gl	a ct u Le	u Gl	y Al	g gt a Va	c aa l Ly	g ta	r va	T GT	g tg u Cy	s Se	r Al	a ctc a Leu 160	•	180
145	<b>a</b> 20		a aa	a tt	15) G aad	oraa	c at	a tt	t ga	t qa	a ac	c at	c gt	c go	e geg		528
Thr	Glr	ı Ly	s Gl	у Le 16	u Ly: 5	s As	n va	II Pn	e As	0 Der	u Aı	.a	e va	17	5		576
ctg Leu	gag Glu	g cc	o Pr	o Va	g gt l Va	g aa l Ly	g aa s Ly	g aa s Ly 18	S GI	y Pr	g aa o Ly	rs Cy	r gt s Va 19		c ctt e Leu	•	0
tga			18	J					. <b>.</b>							* !	579

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                             40
 Asp Pro Tyr Thr Leu Gly Leu Phe Asp Thr Ala Gly Gln Glu Asp Tyr
                         55
Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Val
                                          75
                     70
 Cys Phe Ser Val Thr Ser Pro Ala Ser Phe Glu Asn Val Lys Glu Lys
 Trp Phe Pro Glu Val Arg His His Cys Pro Gly Val Pro Cys Leu Ile
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                                 105
                                                      110
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 Leu Ala Arg Gln Lys Gln Arg Pro Val Thr Ser Asp Gln Gly Glu Arg
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                                             140
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 tacaagetqt teatcateaa atectetetg tgattttett etetgtgeat atattettaa
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                                                                        232
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 Val Val Thr Gly Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile Ser
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                             20
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Tyr Thr Thr Asn Ala Phe Pro Gly Glu Tyr Ile Pro Thr Val Phe Asp
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 aac tat acg get agt gtg atg gta gat ggt agg ccc atc agc ttg gga
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Asn Tyr Thr Ala Ser Val Met Val Asp Gly Arg Pro Ile Ser Leu Gly
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 ctg tgg gat act gct ggg caa gaa gat tat gac cga ctg aga ccg ctg
                                                                        424
Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu
                                     70
tee tae eet caa ace gae gte tte ete ate tge tte tee att gte age
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, 200	3/014	1020						0.4/20	11								
								194/29			<b>5</b> 1	<b>7</b>	<b>*1</b> ~	1707	C^~		
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cct	cct	tcg	ttt	gac	aac	gtc	aag	gca	aag	tgg	tac	ccg	gag	att	gag		520
Pro	Pro	Ser 95	Phe	Asp	Asn	Val	Lys 100	Ala	Lys	Trp	Tyr	Pro 105	GIU	TTE	GIU		
cac	cat	gcc	CCC	aat	gtt	CCC	atc	atc	ctt	gtt	ggt	acc	aaa	ctc	gat		568
His	His 110	Ala	Pro	Asn	Val	Pro 115	Ile	Ile	Leu	Val	Gly 120	Thr	Lys	Leu	Asp		
cta	aga	qac	gat	CCC	gcg	aca	gca	gaa	tcc	ctc	cgg	cag	aaa	aag	atg		616
Leu	Arg	Asp	Asp	Pro	Ala	Thr	Ala	Glu	Ser	Leu	Arg	Gln.	Lys	Lys	Met		
125			-		130					135					140		
gac	cta	tct	cat	acq	aga	cac	taa	ccq	tcg	cca	aaa	gag	atc	cga	gcg		664
Dan.	Leu	Ser	Arg	Thr	Arg	His	Tro	Pro	Ser	Pro	Lys	Glu	Ile	Arg	Ala		
-LOD			3	145			•		150		_			155		•	
cac	aaσ	tat	ctc	σaa	tat	tct	qcc	ctc	agg	caq	cgc	aac	ttc	aaa	agc		712
Hie	Tays	Tvr	Leu	Ğlu	Cvs	Ser	Ăla	Leu	Arg	Gln	Arg	Asn	Phe	Lys	Ser		
1123	_,_	-1-	160					165	_		_		170				
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Va I	Phe	Asp	Glu	Ala	Ile	Arg	Ãla	Val	Leu	Asn	Pro	Gly	Pro	Ala	Ala		
V (2.1		175					180					185					
222	cca	aaσ	agc	aag	aaa	tac	acc	ata	ctg	taga	acca	tta (	cttt	cage	tt		810
Tage	Pro	Tivs	Ser	Lvs	Lys	Cvs	Thr	Ile	Leu	_							
шур	190	,-		-4-	2	195											
ttc	atca	tct a	aatc	ataa	ac a	acta	attc	g gc	gtct	ggga	tag	ttga	agg	tttt	gcaatg		870
											•						
atc	ccct	tga	tgat	tgtt	cc a	actg	tgtt	c at	attt	cttt	ctc	tctt	tct	cggt	cacatg		930
									•								
tca	tgat	cct	gatg	agct	tc t	ttct	gggt	c ag	gaca	cccc	ttt	cctc	atc	ttgt	cgtctt		990
			L			a++~	+	e ta	atac	acca	taa	cadd	ааσ	ctat.	cactta		1050
ttt	grgc	aca	tgca	gcat	aa a	cere	Laac	a Ly	CLAC	gcca	Laa	~~99	~~9		cactta		
atc	gatt	taa	cctc	catt	gt c	ctaa											1075

<210> 258

<211> 198

<212> PRT

<213> Aspergillus fumigatus

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Ala Ile Arg Ala Val Leu Asn Pro Gly Pro Ala Ala Lys Pro Lys Ser 180 185 Lys Lys Cys Thr Ile Leu 195 <210> 259 <211> 594 <212> DNA <213> Aspergillus fumigatus <220> <221> CDS <222> (1)..(594) <400> 259 atg gag ctg tgc ggg cgc cag aaa gtt gtc cag cgc aag atg gta ctc 48 Met Glu Leu Cys Gly Arg Gln Lys Val Val Gln Arg Lys Met Val Leu tta gga gat ggt gct tgc ggc aag acg tca gct ttg aat gtg ttt aca 96 Leu Gly Asp Gly Ala Cys Gly Lys Thr Ser Ala Leu Asn Val Phe Thr aga ggg ttc ttc ccg aca gtc tat gag ccg act gtt ttt gaa aac tat 144 Arg Gly Phe Phe Pro Thr Val Tyr Glu Pro Thr Val Phe Glu Asn Tyr 40 gtc cat gac att ttc gtc gat aac gta cac atg gag ttg tcg ctg tgg 192 Val His Asp Ile Phe Val Asp Asn Val His Met Glu Leu Ser Leu Trp 55 60 gat aca gcc ggt caa gaa gaa ttc gat cga tta cga gca ctg tcc tac 240 Asp Thr Ala Gly Gln Glu Glu Phe Asp Arg Leu Arg Ala Leu Ser Tyr gag gat aca cat gtt att atg cta tgt ttc agc gtc gat agc cct gac 288 Glu Asp Thr His Val Ile Met Leu Cys Phe Ser Val Asp Ser Pro Asp 90 tcg ttc gaa aat gtg gcg acg aaa tgg att gat gag att cgc gag aat 336 Ser Phe Glu Asn Val Ala Thr Lys Trp Ile Asp Glu Ile Arg Glu Asn 100 105 110 tgc ccc ggc gtg aag tta gtc ctc acg gca ctc aaa tgc gat ctg cga 384 Cys Pro Gly Val Lys Leu Val Leu Thr Ala Leu Lys Cys Asp Leu Arg 120 aaa gac gac gag ttg aac gac aac ccg aac gcc atc acg ttc gaa caa 432 Lys Asp Asp Glu Leu Asn Asp Asn Pro Asn Ala Ile Thr Phe Glu Gln 135 gga tta gcg aaa gca aag gaa atc ggc gct gta aaa tac ctt gaa tgc 480 Gly Leu Ala Lys Ala Lys Glu Ile Gly Ala Val Lys Tyr Leu Glu Cys 150 155 tet get gtt eag aat ege ggt ate agg gag ace tit tat gaa gee gee 528 Ser Ala Val Gln Asn Arg Gly Ile Arg Glu Thr Phe Tyr Glu Ala Ala 165 170 aag gtc gct ctt gat gtg aag cct gca gga tcc agc ggg tcc aag gga 576 Lys Val Ala Leu Asp Val Lys Pro Ala Gly Ser Ser Gly Ser Lys Gly 180 cag tgc att atc ctc tga 594 Gln Cys Ile Ile Leu 195 <210> 260 <211> 197 <212> PRT <213> Aspergillus fumigatus <400> 260 Met Glu Leu Cys Gly Arg Gln Lys Val Val Gln Arg Lys Met Val Leu 10 Leu Gly Asp Gly Ala Cys Gly Lys Thr Ser Ala Leu Asn Val Phe Thr Arg Gly Phe Phe Pro Thr Val Tyr Glu Pro Thr Val Phe Glu Asn Tyr

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PCT/EP2004/008136 196/291 Val His Asp Ile Phe Val Asp Asn Val His Met Glu Leu Ser Leu Trp 55 Asp Thr Ala Gly Gln Glu Glu Phe Asp Arg Leu Arg Ala Leu Ser Tyr 75 Glu Asp Thr His Val Ile Met Leu Cys Phe Ser Val Asp Ser Pro Asp 85 Ser Phe Glu Asn Val Ala Thr Lys Trp Ile Asp Glu Ile Arg Glu Asn 105 100 Cys Pro Gly Val Lys Leu Val Leu Thr Ala Leu Lys Cys Asp Leu Arg 125 120 115 Lys Asp Asp Glu Leu Asn Asp Asn Pro Asn Ala Ile Thr Phe Glu Gln 135 Gly Leu Ala Lys Ala Lys Glu Ile Gly Ala Val Lys Tyr Leu Glu Cys 155 150 Ser Ala Val Gln Asn Arg Gly Ile Arg Glu Thr Phe Tyr Glu Ala Ala 170 175 165 Lys Val Ala Leu Asp Val Lys Pro Ala Gly Ser Ser Gly Ser Lys Gly 185 Gln Cys Ile Ile Leu 195 <210> 261 <211> 582 <212> DNA <213> Mus musculus <220> <221> CDS <222> (1)..(582) <400> 261 atg gct gcc atc cgg aag aaa ctg gtg atc gtg gga gat gga gct tgt : 48 Met Ala Ala Ile Arg Lys Lys Leu Val Ile Val Gly Asp Gly Ala Cys 10 gga aaa aca tgt ttg ctc atc gtc ttc agc aag gac cag ttt cct gag 96 Gly Lys Thr Cys Leu Leu Ile Val Phe Ser Lys Asp Gln Phe Pro Glu 25 20 gtt tac gtg ccc aca gta ttt gag aac tat gtg gct gat atc gaa gtg 144 Val Tyr Val Pro Thr Val Phe Glu Asn Tyr Val Ala Asp Ile Glu Val 45 40 gat gga aaa cag gtg gag ttg gcc ctg tgg gat aca gct gga caa gaa Asp Gly Lys Gln Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu 192 55 50 gat tat gat ege etg agg eca etc tec tat ece gac act gat gtt etc 240 Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Thr Asp Val Leu 70 ttg tta tgt ttc tcc att ggc aac cct gat agc ttt ggg aac atc cca 288 Leu Cys Phe Ser Ile Gly Asn Pro Asp Ser Phe Gly Asn Ile Pro 95 90 85 cat aaa tgg att cca gaa gtc aag cat ttc tgt ccc aac gtg ccc atc 336 His Lys Trp Ile Pro Glu Val Lys His Phe Cys Pro Asn Val Pro Ile 110 105 atc ctg gtt ggg agt aag aag gat ctt cgg aat gac ttc tac acg ata 384 Ile Leu Val Gly Ser Lys Lys Asp Leu Arg Asn Asp Phe Tyr Thr Ile 125 120 115 caa gag tta gcc aag agg aag caa gcg cct gtg aga cct gaa caa ggc 432 Gln Glu Leu Ala Lys Arg Lys Gln Ala Pro Val Arg Pro Glu Gln Gly 135 caa ggg ttg gcg aac agc att ggc gct ttc gag tat gtg gag tgt tca 480 Gln Gly Leu Ala Asn Ser Ile Gly Ala Phe Glu Tyr Val Glu Cys Ser 155 150 geg aag acc aaa gat gga gtg agg gtc ttt gaa aag gcc aca agg 528 Ala Lys Thr Lys Asp Gly Val Arg Arg Val Phe Glu Lys Ala Thr Arg

170

576

582

get get etg caa aeg aat ega gtg aag aaa aag aet ggt tge ttt gte

Ala Ala Leu Gln Thr Asn Arg Val Lys Lys Thr Gly Cys Phe Val 185

165

ttt tga

Phe

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105

							_										
Va1	Val	Ala 115	Thr	Gln	Thr	qzA	Gln 120	Arg	Glu	Val	gga Gly	Pro 125	Hls	Arg	Ата	:	384
Ser	Cys 130	Ile	Asn	Ala	Ile	Glu 135	Gly	Lys	Arg	Leu	gcc Ala 140	Gin	Asp	vaı	Arg	•	432
Ala 145	Lys	Gly	Tyr	Leu	Glu 150	Cys	Ser	Ala	Leu	Ser 155	aac Asn	Arg	Gly	Val	Gln 160	•	480
caq	gta Val	ttt Phe	gaa Glu	tgt Cys 165	gct Ala	gtc Val	cga Arg	aca Thr	gct Ala 170	gtc Val	aac Asn	cag Gln	gcc Ala	agg Arg 175	agg Arg		528
cga Arg	aac Asn	aga Arg	agg Arg 180	aag Lys	ctg Leu	ttc Phe	tcc Ser	atc Ile 185	aat Asn	gaa Glu	tgc Cys	aag Lys	atc Ile 190	ttc Phe			573
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<213> Mus musculus

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<210> 265 <211> 786 <212> DNA <213> Mus musculus

180

<220>
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 1
 5
 10
 15

 1
 15
 10
 15

 1
 20
 25
 30
 30

 96
 25
 30
 30
 30

 144
 30
 30
 30
 30

								199/2	91.								
Ala	Arg	Gly 35	Pro	Gly	Val	Ser	Gly 40	Gly	Arg	Gly	Arg	Ala 45	Gly	Gly	Ala		
gaç Glu	gga Gly 50	cgc Arg	ggc	gtc Val	aag Lys	tgc Cys 55	gtg Val	ctg Leu	gtc Val	ggc Gly	gac Asp 60	ggc	gcg Ala	gtg Val	ggc		192
aac Lys 65	acc	agc Ser	ctg Leu	gtg Val	gtc. Val 70	agc Ser	tac Tyr	acc Thr	act Thr	aac Asn 75	ggc	tac Tyr	ccc Pro	acc Thr	gag Glu 80		240
Туз	atc	Pro	Thr	Ala 85	Phe	Asp	Asn	Phe	Ser 90	Ala	Val	Val	Ser	Val 95	qaA		288
G1 <sup>3</sup>	cgg Arg	cct Pro	gtg Val 100	aga Arg	ctc Leu	cag Gln	ctc Leu	tgt Cys 105	gac Asp	act Thr	gca Ala	gga Gly	cag Gln 110	gat Asp	gag Glu		336
ttt Phe	gac Asp	aag Lys 115	ctg Leu	agg Arg	ccc Pro	ctc Leu	tgc Cys 120	tac Tyr	acc Thr	aac Asn	aca Thr	gac Asp 125	atc Ile	ttc Phe	ctg Leu		384
Let	tgc Cys 130	tťċ Phe	agc Ser	gtģ Val	gtg Val	agc Ser 135	ccc Pro	aca Thr	tcc Ser	ttc Phe	cag Gln 140	aac Asn	gtg Val	ggc	gag Glu		432
aag Lys	tgg Trp	gtt Val	cca Pro	gag Glu	att Ile 150	cga Arg	cgt	cac His	tgc Cys	cca Pro 155	Lys	gcc	ccc Pro	atc Ile	atc Ile 160	•	480
cto	gtc Val	gjà aaa	aca Thr	cag Gln 165	tcg Ser	gac Asp	ctc Leu	agg Arg	gag Glu 170	gac Asp	gtc Val	aaa Lys	gtg Val ·	ctc Leu 175	ata Ile		528
gaa Glu	ctg Leu	gac Asp	aag Lys 180	tgc Cys	aaa Lys	gag Glu	aag Lys	ccg Pro 185	gtg Val	ect Pro	gaa Glu	gag Glu	gcg Ala 190	gcg Ala	aag Lys		576
cto Lev	tgc Cys	gcg Ala 195	gag Glu	gaa Glu	gtc Val	aaa Lys	gct Ala 200	gtc Val	tcc Ser	tac	atc Ile	gag Glu 205	tgc Cys	tca Ser	gcg Ala		624
tto	act Thr 210	Gln	aaa Lys	aac Asn	ctc Leu	aaa Lys 215	gag Glu	gtt Val	ttc Phe	gac Asp	gcc Ala 220	gcc	att Ile	gtt Val	gct Ala		672
ggt G1; 225	atc Ile	cag Gln	cac His	tca Ser	gac Asp 230	tcc Ser	cag Gln	cta Leu	cag Gln	cca Pro 235	aag Lys	aag Lys	tct Ser	aaa Lys	agc Ser 240		720
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	tgc Cys				tga											•	786

<210> 266 <211> 261 <212> PRT

<213> Mus musculus

260

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	Cys 1	Phe	Ser '	Val		Ser 135	Pro	Thr	Ser	Phe	Gln 140	Asn	Val	Gly	Glu		
Lys	Trp '				150					155					TP0		
Leu	Val (			165					170					175			
	Leu :		180					185					190				
	Cys	195					200					205					
	Thr 9					215					220						
225	Ile				230					235					240		
_	Thr			245	Val	Arg	Asp	Leu	Ser 250	Lys	ser	Trp	Trp	255	гуз		
Tyr	Cys	Cys	Leu 260	Ala			··						•	•			٠
<211 <212	)> 26 .> 62 !> DN !> Tr	4 [A	oderm	a re	eesei	L											
<220																	
	L> CD 2> (1		(624)		•			•									
<400	> 26	<b>57</b> .				_							ata	~++	att		48
Met	cct Pro	ctc Leu	tgc Cys	ggc 5	GJÀ	Ser	aag Lys	acg	yal 10	Gln	Arg	Lys	Leu	Val 15	Leu	•	*0
ctg	ggc Gly	gat	ggt	gcc	agc Ser	gga Glv	aag Lvs	acg Thr	tcg	ctg Leu	ctc Leu	aac Asn	gtc Val	ttc Phe	aca Thr	* :	96
	ggt		20					25					30			;	144
Arg	Gly	Tyr 35	Phe	Pro	Thr	Val	Tyr 40	Glu	Pro	Thr	vaı	Pne 45	GIU	ASII	туг		
Val	cac His 50	Ąsp	Ile	Phe	Val	Asp 55	Asn	Val	His	Ile	60 GIu	Leu	ser	ren	Trp		192
gat Asp 65	acg Thr	gcg Ala	gga Gly	cag Gln	gag Glu 70	gaa Glu	ttc Phe	gat Asp	cgg	ctg Leu 75	cga Arg	tcg Ser	ctc Leu	tcc Ser	tac Tyr 80		240
σa t	gac Asp	acc Thr	gat Asp	ttg Leu 85	atc	gtg Val	ctc Leu	tgt Cys	tac Tyr 90	tcg Ser	gtc Val	gat	agc Ser	aaa Lys 95	gac	•	288
tcg Ser	cta Leu	gaa Glu	aac Asn 100	atc	gaa Glu	tcc Ser	aaa Lys	tgg Trp	gto Val	gga Gly	gag Glu	att	gcc Ala 110	Asp	aac Asn	,	336
tgc Cys	ccc Pro	ggc Gly 115	gtc Val	aag Lys	ctg Leu	gtc Val	cto Lev	gto Val	geo	Lev	aag Lys	tgc Cys 125	Asp	ctg Leu	cgc Arg		384
Gln	Gln 130	gag Glu	gac Asp	Asp	Glu	135	gag Glu	gao 1 Asp	Glr	ı Ala	140	) LALē	L ASP	GIA	aac Asn		432
Ala	Gln	Arg	Glu	Lys	9rc	Pro	Thi	: Ile	e Ser	Ty:	: Asy	) GII	ı Gıy	Leu	gag Glu 160		480
ato	acc	aag Lys	cgg Arg	ata Ile	ggc Gly	gec	tco Ser	g cgo	tac Tyi	: Let	g gag ı Glu	tgo Cys	tcg Ser	gcg Ala	atg Met		528
aag Lys	aac Asn	cgc	, Gly	gto Val	aac	gaç Glu	g gco 1 Ala	tti a Phe 18	e Thi	gag	g gcg	g gco a Ala	c cgc a Arg 190	gta y Val	gcg L Ala		576
cta Lev	agc Ser	gto Val	. Lys	aac	g gag s Gli	g agg	g gaa g Gli 20	a gad u Asj	c aac	c aaq n Lys	g tge s Cy:	aca Th: 20!	a ato r Ile	ate	ਤ =		621

624

taa

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<211> 207
<212> PRT
<213> Trichoderma reesei
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Arg Gly Tyr Phe Pro Thr Val Tyr Glu Pro Thr Val Phe Glu Asn Tyr
Val His Asp Ile Phe Val Asp Asn Val His Ile Glu Leu Ser Leu Trp
Asp Thr Ala Gly Gln Glu Glu Phe Asp Arg Leu Arg Ser Leu Ser Tyr
Asp Asp Thr Asp Leu Ile Val Leu Cys Tyr Ser Val Asp Ser Lys Asp
Ser Leu Glu Asn Val Glu Ser Lys Trp Val Gly Glu Ile Ala Asp Asn
             100
                                  105
Cys Pro Gly Val Lys Leu Val Leu Val Ala Leu Lys Cys Asp Leu Arg
         115
                              120
Gln Gln Glu Asp Asp Glu Pro Glu Asp Gln Ala Ala Ala Asp Gly Asn
                          135
Ala Gln Arg Glu Lys Pro Pro Thr Ile Ser Tyr Asp Glu Gly Leu Glu
                                          155
                     150
Val Ala Lys Arg Ile Gly Ala Ser Arg Tyr Leu Glu Cys Ser Ala Met
                                      170
Lys Asn Arg Gly Val Asn Glu Ala Phe Thr Glu Ala Ala Arg Val Ala
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Leu Ser Val Lys Lys Glu Arg Glu Asp Asn Lys Cys Thr Ile Met
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<211> 675
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Lys Ile Val Ile Leu Gly Asp Gly Ala Cys Gly Lys Thr Ser Leu Leu
aac gtg ttc acg cga ggg tac ttt ccg aag gtg tac gag ccc acg gta
                                                                          144
Asn Val Phe Thr Arg Gly Tyr Phe Pro Lys Val Tyr Glu Pro Thr Val
                              40
                                                   45
ttc gaa aac tac atc cat gac atc ttc gtg gac aac cag cac atc acg
                                                                          192
Phe Glu Asn Tyr Ile His Asp Ile Phe Val Asp Asn Gln His Ile Thr
                         55
                                               60
ctg agc ctg tgg gac act gct ggg cag gag ttt gac cgg ttg cga
                                                                          240
Leu Ser Leu Trp Asp Thr Ala Gly Gln Glu Glu Phe Asp Arg Leu Arg
                     70
                                          75
tcg ctg tcg tac tcg gac aca cac acg att atg ctg tgt ttc tcg gtg
Ser Leu Ser Tyr Ser Asp Thr His Thr Ile Met Leu Cys Phe Ser Val
                                                                          288
                                      90
gac tcg cgg gac tcg ctg gag aac gtc aag aac aag tgg gtg agc gaa
Asp Ser Arg Asp Ser Leu Glu Asn Val Lys Asn Lys Trp Val Ser Glu
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att	gcg	gac	cac	tgc	gag	ggc	gtg	aag	ctg	gtg	cta	gtg	gcg	ctg	aag	384
Ile	Ala	Asp 115	His	Cys	Glu	Gly	Val 120	Lys	Leu	Val	Leu	Val 125	Ala	Leu	гуз	
tgc	gac	ttg	cgc	agc	agc	gac	gag	tac	agc	aac	gag	agc	gcc	atc	acg	432
-	130					135					Glu 140					
ccg	ggg	tcc	atc	cag	aac	cag	aag	tac	aac	ggc	ggc	ggc	ggc	aac	aaa	480
Pro	Gly	Ser	Ile	Gln		Gln	Lys	Tyr	Asn.		Gly	Gly	Gly	Asn	GTA	
145					150					155					160	FOO
ctg	atc	CCC	tac	gac	gag	<u>a</u> aa	ctg	gcg	atg	gcc	aag	cag	att	999	gcg	528
				165					170		Lys			175		
ctg	cgc	tat	ctg	gag	tgc	agc	gcc	aag	atg	aac	cgt	ggc	gtg	aac	gag	576
Leu	Arg	Tyr	Leu 180	Glu	Cys	Ser	Ala	Lys 185	Met	Asn	Arg	Gly	Val 190	Asn	GIU	
gcg	ttc	acc	gag	gct	gcg	cgc	tgc	gcg	ctg	act	gcg	aca	ccg	aag	āāa	624
		195					200				Ala	205				
gcc	cgg	gac	tct	gcg	CCC	gag	gcc	gaa	agc	agc	agt	tgt	act	atc	atg	672
Āla	Arg	Asp	Ser	Ala	Pro	Glu 215	Ala	Glu	Ser	Ser	Ser 220	Cys	Thr	Ile	Met	
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tga																

<210> 270 <211> 224 <212> PRT <213> Ashbya gossypii

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<210> 271 <211> 624 <212> DNA

<213> Ashbya gossypii

203/291 <221> CDS

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gtc	gga Gly	gat Asp	ggt Gly 20	gca Ala	tgc Cys	eja aaa	aaa Lys	aca	tgt	ctt Leu	ttg Leu	att	gtg Val 30	ttt	gcc Ala		96
aag Lys	gga Gly	aag Lys 35	ttc	cca Pro	cag Gln	gtg Val	tat Tyr	gtt	cct Pro	acg Thr	gtt Val	ttc Phe 45	gac	aac Asn	tac Tyr		144
gtt Val	gca Ala 50	gat	gtg Val	gag Glu	gta Val	gac Asp 55	Gly	aga Arg	cgg Arg	gtg Val	gag Glu 60	ctt	gcg Ala	ctt Leu	tgg Trp		192
gat Asp 65	acg Thr	gct Ala	GJA GGA	cag Gln	gag Glu 70	gat Asp	tac Tyr	gac Asp	agg Arg	cta Leu 75	cgg	ecg Pro	tta Leu	tcg Ser	tac Tyr 80	•	240
cca Pro	gac Asp	tcc Ser	aat Asn	gtt Val 85	gtg Val	ttg Leu	atc Ile	Cys	tac Tyr 90	tcg Ser	att Ile	gac Asp	cta Leu	cca Pro 95	gac Asp		288
Ser	ttg Leu	Glu	Asn 100	Val	Met	Glu	Lys	Trp 105	Ile	Ser	Glu	Val	Leu 110	Tyr	Phe		336
Cys	cag Gln	Gly 115	Val	Pro	Ile	Ile	Leu 120	Val	Gly	Сув	Lys	Ala 125	Asp	Leu	Arg	. · .	384
aac Asn	gat Asp 130	ccg Pro	caa Gln	gtg Val	atc Ile	gag Glu 135	cag Gln	ttg Leu	aga Arg	cag Gln	cag Gln 140	gga Gly	cag Gln	cag Gln	cct Pro		432
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tag															•		624

<210> 272 <211> 207 <212> PRT

<213> Ashbya gossypii

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Cys Gln Gly Val Pro Ile Ile Leu Val Gly Cys Lys Ala Asp Leu Arg 120 115 Asn Asp Pro Gln Val Ile Glu Gln Leu Arg Gln Gln Gly Gln Gln Pro 140 130 135 Val Ser Gln Ala Gln Ala Gln Glu Val Ala Asp Gln Ile Gly Ala Val 150 155 Glu Tyr Ile Glu Cys Ser Ala Lys Thr Gly Phe Gly Val Arg Glu Val 170 165 Phe Glu Ala Ala Thr Arg Ala Ser Leu Met Gly Lys Gln Gly Lys Ser 185 190 180 Lys Ala Lys Ser Asp Lys Lys Lys Lys Lys Cys Val Val Leu 200 195

<210> 273 <211> 615 <212> DNA <213> Yarrowia lipolytica

<221> CDS

<222> (1)..(615)

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<210> 274 <211> 204

<212> PRT

<213> Yarrowia lipolytica

### 205/291.

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qcc	160 atc	aag	gta	gta	atc	165 agg	cct	ccg	acg	aag	170 cag	cga	gaa	agg	aag	579
175		-	Val		180					185					190	
aaa Lys	aag Lys	aaa Lys	gaa Glu	Arg	cga Arg	gga Gly	tgc Cys	tca Ser	Ile 200	Phe	Cys	agc Ser	Arg	Ile 205	Met	627
			aga Arg						tgat	cagaa	agg (	cctt	ette			674
			210					215		tata	gtti	gtct	ccc a	atgt	tccaaa	734
gtgo 	ctcgi	ttg (	egeti	tgtg	ca ci	ttgg	gctgg	g taa	atgt	gtat	atti	tagto	ett 1	tgcc	aattga	 794
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gtc	caati	aca i	tact	aagaa	ag ta	aacaa	atati	t tt	cttc	cgat	gati	tttai	tta '	tggt	ttctcg	914
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<210> 277 <211> 1002 <212> DNA

207/291 <213> Zea mays

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            20
Thr Asp Tyr Ile Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Ser
        35
                            40
Val Asp Gly Ser Ile Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln
                                            60
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Glu Asp Tyr Ser Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val
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Phe Val Leu Ala Phe Ser Leu Ile Ser Arg Ala Ser Tyr Glu Asn Val
                                    90
Leu Lys Lys Trp Val Pro Glu Leu Arg Arg Phe Ala Pro Asp Val Pro
            100
                                105
                                                    110
Val Val Leu Val Gly Thr Lys Leu Asp Leu Arg Asp His Arg Ala Tyr
                                                 125
                            120
        115
Leu Ala Asp His Pro Gly Ala Ser Thr Ile Thr Thr Ala Gln Gly Glu
                                            140
                        135
Glu Leu Arg Arg Gln Ile Gly Ala Ala Ala Tyr Ile Glu Cys Ser Ser
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                                        155
Lys Thr Gln Gln Asn Val Lys Ser Val Phe Asp Thr Ala Ile Lys Val
                                     170
                                                         175
                165
Val Leu Gln Pro Pro Arg Arg Arg Glu Ala Thr Pro Ala Arg Arg Lys
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Thr Cys Ala Ala
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<213> Oryza sativa
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                                                          Met Ser
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geg tet egg tte ate aag tge gte ace gtg ggg gae gge gee gtg gge
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Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala Val Gly
                             10
                                                 15
aag acc tgc atg ctc atc tcc tac acc tcc aac acc ttc ccc acg gac
                                                                        213
Lys Thr Cys Met Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro Thr Asp
                         25
                                             30
 tat gtt cca act gtt ttt gat aac ttc agt gca aat gtt gtg gtc gat
                                                                        261
 Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val Val Asp
                                        45
                     40
                                                                        309
 qqq aqc act gtg aac ttg ggg ttg tgg gat aca gca gga caa gag gac
 Gly Ser Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp
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                                     60
 tac aat agg cta cgc ccg ttg agc tat cgt ggc gct gat gtt ttc ctg
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 Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp Val Phe Leu
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 ctg gcc ttt tct ctg atc agc aaa gca agc tat gag aat gtt tct aaa
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#### 209/291 Leu Ala Phe Ser Leu Ile Ser Lys Ala Ser Tyr Glu Asn Val Ser Lys 90 aag tgg ata cct gaa tta agg cat tat gct cct ggt gtg cca ata att 453 Lys Trp Ile Pro Glu Leu Arg His Tyr Ala Pro Gly Val Pro Ile Ile 105 110 ctc gtt gga aca aag ctt gat ctg cgg gat gat aag caa ttt ttc gta 501 Leu Val Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Gln Phe Phe Val 115 120 125 gat cac cct ggt gct gta cct att tcc act gct cag ggc gaa gag ctg Asp His Pro Gly Ala Val Pro Ile Ser Thr Ala Gln Gly Glu Glu Leu 549 135 140 agg aaa ctc att ggt gca gcg gca tac att gaa tgc agt tca aaa aca 597 Arg Lys Leu Ile Gly Ala Ala Ala Tyr Ile Glu Cys Ser Ser Lys Thr 150 155 cag caa aac atc aag gca gtt ttc gat gct gcg att aag gtg gtt ctc 645 Gln Gln Asn Ile Lys Ala Val Phe Asp Ala Ala Ile Lys Val Val Leu 170 175 cag cct cca aag caa aag aag aag aaa aag gcg cag aaa gga tgt 693 Gln Pro Pro Lys Gln Lys Lys Lys Lys Lys Ala Gln Lys Gly Cys 185 190 gcc atc ttg taattaaatg gtagacagtg cagtgcagat cgatgtatcc cttcatttgt 752 Ala Ile Leu agectetgge tteaategte gettgtttgt ataattaege tagatgeeac eggeagaaga 812 tataatatag tecteetgee tttgtggtgt tggtetet 850

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<210> 281 <211> 800 <212> DNA <213> Suillus bovinus

Gly Cys Ala Ile Leu 195

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М	ga atg cac aac atc aaa tgt gtt gta gtc ggc gat ggt gct gtt ggc Met His Asn Ile Lys Cys Val Val Val Gly Asp Gly Ala Val Gly 1 5 10 15 aag acg tgt ctt ctc atc tct tat acc aca aat gcc ttt cca gga gaa															167
aag Lys	acq	tgt Cys	ctt Leu	ctc Leu 20	atc Ile	tct Ser	tat Tyr	acc Thr	aca Thr 25	aat Asn	gcc Ala	ttt Phe	cca Pro	gga Gly 30	gaa Glu	215
tac Tyr	gtg Val	cca Pro	aca Thr 35	qta	ttc Phe	gac Asp	aac Asn	tac Tyr 40	tct Ser	gca Ala	aat Asn	gtg Val	atg Met 45	gtc Val	gac Asp	263
ggg Gly	aaa Lys	act Thr 50	atc	tct Ser	ctc Leu	ggt Gly	cta Leu 55	tgg Trp	gat Asp	acc Thr	gct Ala	gga Gly 60	caa Gln	gaa Glu	gat Asp	311
Tyr	Asp 65	cgt Arg	Leu	Arg	Pro	Leu 70	Ser	Tyr	Pro	Gln	Thr 75	Asp	gtc Val	Phe	Leu	359
Ile 80	tgt Cys	Phe	Ser	Leu	Val 85	Ser	Pro	Pro	Ser	Tyr 90	Glu	Asn	gtt Val	Arg	Thr 95	407
aag Lys	Trp	Trp	Pro	Glu 100	Ile	Ser	His	His	Ala 105	Pro	Ser	Thr	tcg Ser	Val 110	Val	455
Leu	Val	Gly	Thr 115	Lys	Leu	Asp	Leu	Arg 120	Glu	Asp	Pro	Ala	acc Thr 125	TTE.	GIU	503
Lys	Leu	Arg	Asp	Arg	Arg	Met	Gln 135	Pro	Ile	Gln	Tyr	140		GIĀ	vaı	551
Ser	Met	Ala	Arg	Asp	Ile	Gly 150	Ala	Val	Lys	Tyr	Leu 155	Glu	tgt Cys	ser	Ala	599
Leu 160	Ser	Gln	Lys	Gly	Leu 165	ГÀЗ	Thr	Val	Phe	Asp 170	Glu	Val	atc	Arg	175	647
gtt Val	Leu	Asn	Pro	Pro 180	Pro	Lys	Glu	Lys	Lys 185	Arg	Ser	Gly	cgt Arg	190	Cys	695
	atc Ile				att	tgcc	attc	ca c	atgc	tcat	a ta	gatg	gatt	ttc	tttgttt	754
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	Суз	Phe	: Ser	Leu	Val 85		Pro	Pro	Ser	Tyr 90		Asn	Val	Arg	Thr 95	Lys		
	Trp	Trp	Pr <sub>i</sub> o	Glu 100	Ile	Ser	His	His	Ala 105		Ser	Thr	Ser	Val	Val	Leu		
•	Val	Gly	Thr 115	Lys	Leu	Asp	Leu	Arg		Asp	. Pro	Ala	Thr 125	Ile		Lys		
	Leu	Arg 130	Asp	Arg	Arg	Met	Gln 135		Ile	Gln	Tyr	Thr 140			Val	Ser		•
	145		Arg			150					155				+,	160		
			Lys		165					170				_	175			
			Pro	Pro 180	Pro	Lys	Glu	Lys	Lys 185		Ser	Gly	Arg	Gly 190	Сув	Val		
	ile	Val																
		0> 2							•		•	•		: .			•	
	<21	1> 1 2> D		ıa b	~~~													
	<21.	3 > 5	ulli	ra Do	OATH	ıs										•		
	<22	0>			٠.												•	.•
		1> C	DS							•								•
	<22	2> (	<u>170)</u>	(74	<b>£</b> 5)								•				•	
				• •														
	-10		02															
	<40			acaco	atao	et ti	ctca	attt	a tta	ctaco	cgac	atci	rtati	-ca	raaat	rtagar	•	60
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	gcc	aaca	tcg a		٠			+								Ŧ		60
	gcc	aaca	tcg a		٠			+								ttagag		60
	gcc	aaca	tcg a		٠			+								Ŧ		
	gcc	aaca	tcg a	etgto	gtga	at to	gggtt	caata	a gca	attto	cctc	gcti	:caa	etc (	tcct	Ŧ	i.	
	gcc	aaca	tcg a	etgto	gtga	at to	gggtt	caata	a gca	attto	cctc	gcti	:caa	etc (	tcct	ecttga	· ·	120
	gcca tcaa atti	aaca acct ttcc aag	tcg atct	etgto agaat gta	gtga cgcd	at to	gggtt gttta	aata atcad	a gca c gta ggt	attto - agaad gct	cctc ccat gta	geti	ccaac aacga aag	etc de ad Me	teete tg ea et G:	ecttga ag act In Thr	· ·	120
	gcca tcaa atti	aaca acct ttcc aag	tcg a	etgto agaat gta	gtga cgcd	at to	gggtt gttta	aata atcad	a gca c gta ggt	attto - agaad gct	cctc ccat gta	gcti	ccaac aacga aag	etc de ad Me	teete tg ea et G:	ecttga ag act In Thr	:	120 178
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	attattattattattattattattattattattattatt	acct ttcc aag Lys s atc Ile	tcg att cat cat ser gat	gta Val tac Tyr	gtg gtg Val acc Thr	gtg Val acg Thr 25 gct	gggtt gttta ggg Gly 10 aac Asn	gac Asp aaa Lys	ggt ggt Gly ttt Phe	attto agaac gct Ala cca Pro	gta Val agc ser 30	gcti ctca ggc Gly 15 gac Asp	aag Lys tat Tyr	ac at Me 1 act Thr gtt Val	tg call tgt Cys ccg Pro	ecttga ag act In Thr ttg Leu act Thr 35	:	120 178 226
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act	tgt	ctc	ctc	atc	tca	tac	aca	aca	aac	aag	ttc	ccc	tct	gaa	tac		96
•			20					25					30		_		
Val	Pro	Thr 35	Val	Phe	Asp	Asn	Tyr 40	Ala	Val	Thr	Val	Met 45	Ile	Gly	Asp		144
gag Glu	Pro 50	tac Tyr	aca Thr	ctc Leu	gga Gly	ctg Leu 55	ttc Phe	gac Asp	acc Thr	gcc Ala	ggt Gly 60	cag Gln	gag Glu	gat Asp	tac Tyr		192
gac Asp 65	cga Arg	ctg Leu	cga Arg	cct Pro	ctt Leu 70	tgt Cys	tac Tyr	cct Pro	cag Gln	acc Thr 75	gat Asp	gtt Val	ttc Phe	ctc Leu	gtc Val 80		240
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tgg Trp	ttc Phe	cct Pro	gag Glu 100	gtc Val	cac His	cac His	cac His	tgc Cys 105	CCC Pro	ggc Gly	gtg Val	cct Pro	tgc Cys 110	ctc Leu	att Ile		336
gtt Val	ggt Gly	acc Thr 115	cag Gln	gtt Val	gat Asp	ccg Pro	cga Arg 120	agt Ser	gac Asp	agg Arg	atg Met	att Ile 125	ctt Leu	gac Asp	aag Lys		384
																	432
Leu															Leu		480
				Leu					Āsp				Val	Āla	gct.		528
		Pro	Pro	gtg				Asn	aaa				gtg Val	ctc		٠	573
tag			-200			٠.		-03	•				190				576
	atg Met 1 act Thr gtt Val gag Glu gasp tty gtt Val tty cteu cteu cteu cteu cteu cteu	atg cag Met Gln 1 act tgt Thr Cys gtt ccc Val Pro gag ccc Glu Pro 50 gac cga Asp Arg 65 tgc ttt Cys Phe tgg ttc Trp Phe gtt ggt Val Gly ctt tcc Leu Ser 130 ctc gcc Leu Ala 145 act cag Thr Gln ctt gag Leu Glu	Met Gln Thr  act tgt ctc Thr Cys Leu  gtt ccc acc Val Pro Thr  35 gag ccc tac Glu Pro Tyr  50 gac cga ctg Asp Arg Leu 65 tgc ttt tcc Cys Phe Ser  tgg ttc cct Trp Phe Pro  gtt ggt acc Val Gly Thr  115 ctt tcc cga Leu Ser Arg 130 ctc gcc cga Leu Ala Arg 145 act cag aag Thr Gln Lys ctt gag cct Leu Glu Pro	atg cag acc ata Met Gln Thr Ile 1 act tgt ctc ctc Thr Cys Leu Leu 20 gtt ccc acc gtt Val Pro Thr Val 35 gag ccc tac aca Glu Pro Tyr Thr 50 gac cga ctg cga Asp Arg Leu Arg 65 tgc ttt tcc gtc Cys Phe Ser Val tgg ttc cct gag Trp Phe Pro Glu 100 gtt ggt acc cag Val Gly Thr Gln 115 ctt tcc cga cac Leu Ser Arg His act cag aag ggt Thr Gln Lys Gly ctt gag cct cca Leu Glu Pro Pro 180	atg cag acc ata aaa Met Gln Thr Ile Lys 1 act tgt ctc ctc atc Thr Cys Leu Leu Ile 20 gtt ccc acc gtt ttt Val Pro Thr Val Phe 35 gag ccc tac aca ctc Glu Pro Tyr Thr Leu 50 gac cga ctg cga cct Asp Arg Leu Arg Pro 65 tgc ttt tcc gtc acc Cys Phe Ser Val Thr 85 tgg ttc cct gag gtc Trp Phe Pro Glu Val 100 gtt ggt acc cag gtt Val Gly Thr Gln Val 115 ctt tcc cga cac aag Leu Ser Arg His Lys 130 ctc gcc cga gaa ctc Leu Ala Arg Glu Leu 145 act cag aag ggt ctc Thr Gln Lys Gly Leu 165 ctt gag cct cca gtg Leu Glu Pro Pro Val 180	atg         cag         acc         ata         aaa         tgt           Met         Gln         Thr         Ile         Lys         Cys           1         5         5         1         1         acc         cys         1         1         5         1	atg         cag         acc         ata         aaa         tgt         gtt           Met         Gln         Thr         Ile         Lys         Cys         Val           act         tgt         ctc         ctc         atc         tca         tac           Thr         Cys         Leu         Leu         Ile         Ser         Tyr           gt         ccc         acc         gtt         ttt         gac         aac           Val         Pro         Thr         Val         Phe         Asp         Asn           35         gag         cct         gga         ctg         ctg         cga         ctg         ctg         cga         ctg         ctg         cga         ctg         ctg         ctg         ctc         ctt         tgt         cys         ro         ro	atg cag acc       ata aaa tgt gtt gtt         Met Gln Thr Ile Lys Cys Val Val         1       5         act tgt ctc ctc atc tca tac aca         Thr Cys Leu Leu Ile Ser Tyr Thr         20         gtt ccc acc gtt ttt gac aac tat         Val Pro Thr Val Phe Asp Asn Tyr         35       40         gag ccc tac aca ctc gga ctg ttc         Glu Pro Tyr Thr Leu Gly Leu Phe         50         gac cga ctg cga cct ctt tgt tac         Asp Arg Leu Arg Pro Leu Cys Tyr         65         tgc ttt tcc gtc acc tct ccc gcc         Cys Phe Ser Val Thr Ser Pro Ala         85         tgg ttc cct gag gtc cac cac cac         Trp Phe Pro Glu Val His His His         100         gtt ggt acc cag gtt gat ccg cga         Val Gly Thr Gln Val Asp Pro Arg         115       120         ctt tcc cga cac aag ctg cga ccc         Leu Ser Arg His Lys Leu Arg Pro         130         ctc gcc cga gaa ctc ggt gcc gtc         Leu Ala Arg Glu Leu Gly Ala Val         145         act cag aag ggt ctc aag gac gtt         Thr Gln Lys Gly Leu Lys Asp Val         165         ctt gag cct cca gtg gtc aag aag         Leu Ala Pro Hele	atg       cag       acc       ata       aaa       tgt       gtt       gtt       gtc         Met       Gln       Thr       Ile       Lys       Cys       Val       Val       Val         1       5       tca       tca       tac       aca       aca       aca         Thr       Cys       Leu       Ile       Ser       Tyr       Thr       Thr </th <th>atg         cag         acc         ata         aaa         tgt         gtt         gtc         ggc           Met         Gln         Thr         Ile         Lys         Cys         Val         Val         Val         Gly           1         ct         tgt         ctc         atc         tca         tac         aca         aca</th> <th>4400&gt; 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aag cag cag cgg gac ccg cag gcg cag tct tac aag cgg gtg cgc aag 950

Lys Gln Gln Arg Asp Pro Gln Ala Gln Ser Tyr Lys Arg Val Arg Lys
240
245
250

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His Arg Cys Val Val Leu
255

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1058

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Val Val Leu

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agc aac aag ttc ccc act gac tac ata cca acg gtg ttc gac aat ttc Ser Asn Lys Phe Pro Thr Asp Tyr Ile Pro Thr Val Phe Asp Asn Phe 30 45	265													
age gea aac gtt gtt gtg gac age ace acg gtg aat etg gge ete tgg Ser Ala Asn Val Val Val Asp Ser Thr Thr Val Asn Leu Gly Leu Trp 50 55 60	313													
gat act gct ggg caa gag gat tac aac cgg ctc agg cct ctg agc tat Asp Thr Ala Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr 65 70 75	361													
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agc tat gaa aat att atg aag aag tgg ata ccg gag cta cag cat tat Ser Tyr Glu Asn Ile Met Lys Lys Trp Ile Pro Glu Leu Gln His Tyr 95 100 105	457													
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gaa gac aag cac tac ttg ttg gac cat cct ggc atg ata cct gtt acc Glu Asp Lys His Tyr Leu Leu Asp His Pro Gly Met Ile Pro Val Thr 130 135 140	<b>553</b>													
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gct gct atc aag gta gta atc cag cct cca act aag cag agg gaa aag Ala Ala Ile Lys Val Val Ile Gln Pro Pro Thr Lys Gln Arg Glu Lys 175 180 185	697													
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461

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Ala	Ser	Tyr	Glu 95	Asn	Val	Leu	Lys	Lys 100	Trp	Met	Pro	Glu	Leu 105	Arg	Arg	
Phe	gca Ala	Pro 110	Asn	Val	Pro	Ile	Val 115	Leu	Val	Gly	Thr	Lys 120	Leu	Asp	Leu	509
cgt Arg	gac Asp 125	cac His	aga Arg	tct Ser	tac Tyr	ctt Leu 130	gcg Ala	gac Asp	cat	cct Pro	gct Ala 135	gct Ala	tcc Ser	gca Ala	att Ile	557
acg Thr 140	act Thr	gca Ala	cag Gln	ggt Gly	gaa Glu 145	gaa Glu	ctt Leu	aga Arg	aag Lys	cag Gln 150	ata Ile	ggc	gcc Ala	gcg Ala	gcc Ala 155	605
Tyr	atc Ile	Glu	Cys	Ser 160	Ser	Lys	Thr	Gln	Gln 165	Asn	Ile	Lys	Ala	Val 170	Phe	653
gat Asp	act	gcc Ala	atc Ile 175	aag Lys	gtg Val	gtc Val	ctt Leu	cag Gln 180	cct Pro	cct Pro	cgg Arg	aga Arg	agg Arg 185	GJÀ aaa	gag Glu	701
acg	Thr	atg Met 190	gca Ala	agg Arg	-aag Lys	aag Lys	aca Thr 195	ağg Arg	cga Arg	agc Ser	acc Thr	ggc Gly 200	tgc Cys	tcg Ser	tta Leu	749
	aac Asn 205										tag	gacci	tgt (	ctgaa	attott	802
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### 221/291. 50 aca gcc ggt caa gag gat tat gat aga ttg cgt cct ctt tca tat ccg 244 Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro 65 292 caa aca gat gta ttt tta gtg tgc ttt tct gtc gtt gca cct tca tct Gln Thr Asp Val Phe Leu Val Cys Phe Ser Val Val Ala Pro Ser Ser ttc gaa aat gtg aaa gag aag tgg gtg ccg gag ata gca cat cac tgc 340 Phe Glu Asn Val Lys Glu Lys Trp Val Pro Glu Ile Ala His His Cys 95 100 388 atg aag aca ccg ttc ctg ctg gtc gga act cag att gat ctt cgt gac Met Lys Thr Pro Phe Leu Leu Val Gly Thr Gln Ile Asp Leu Arg Asp 110 115 gat cct tcc tac atc gaa aaa ttg gca aaa atc aag caa cga cca att 436 Asp Pro Ser Tyr Ile Glu Lys Leu Ala Lys Ile Lys Gln Arg Pro Ile 125 130 aca ttc gaa gtt gga gag aag tta gcg aaa gaa tta aag gca gtg aaa 484 Thr Phe Glu Val Gly Glu Lys Leu Ala Lys Glu Leu Lys Ala Val Lys tac gtc gaa tgt tct gca ctc aca cag aaa ggt cta aaa aat gta ttt 532 Tyr Val Glu Cys Ser Ala Leu Thr Gln Lys Gly Leu Lys Asn Val Phe 160 165 580 gat gaa gca ata ctg gca gca ttg gaa cca ccg gca cag gag aaa aag Asp Glu Ala Ile Leu Ala Ala Leu Glu Pro Pro Ala Gln Glu Lys Lys 175 180 185 aag aaa tgt act ata ctt tagcatcatt gtttctcgat cacgttatat 628 Lys Lys Cys Thr Ile Leu 190 tgatttctga tttgttagtc atttatctgt aaatgattat gttaacgtct taaatgctgc 688 acataccatt actacgtccc ctcttctggt tggtccatct gcgcatatgt gtagtgtttc 748 catctatgcg atatacgtgt agaatgaatg tattcctgta caaaaaaaaa aaaaaaa 805

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<211> 191

<212> PRT

<213> Wuchereria bancrofti

<400> 296

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185

190

222/291

180

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<213> Emericella nidulans
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Leu Ile Val Gly Thr Gln Val Asp Leu Arg Asp Asp Pro Ala Val Arg
                              120
Asp Lys Leu Ala Arg Gln Lys Met Gln Pro Ile Arg Lys Glu Asp Gly
                          135
Asp Arg Met Ala Lys Asp Leu Gly Ala Val Lys Tyr Val Glu Cys Ser
                     150
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Ala Leu Thr Gln Tyr Lys Leu Lys Asp Val Phe Asp Glu Ala Ile Val
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Ala Ala Leu Glu Pro Ala Pro Lys Lys Arg Ser Arg Cys Val Leu Leu
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gtc gga aag acc tgc atg cta atc tcc tac acg aca gac tgc ttt ccc
                                                                            96
Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Thr Asp Cys Phe Pro
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ggc gaa tat gtg ccc aca gtc ttc gac aac tac tcg gcg ccc atg caa
                                                                            144
Gly Glu Tyr Val Pro Thr Val Phe Asp Asn Tyr Ser Ala Pro Met Gln
        35
                              40
                                                   45
gtg gac aca ata cag gtc tcg ctg gga ctg tgg gat acg gcg ggt cag
Val Asp Thr Ile Gln Val Ser Leu Gly Leu Trp Asp Thr Ala Gly Gln
                                                                            192
                          55
gag gac tac gac cgc ctg aga ccg cta tcc tac ccg cag aca gac gtt
                                                                            240
Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val
                                           75
ttc ctg ata tgc tac agc gtg gcg agt ccc tcg tcc ttt gag aac gtc
Phe Leu Ile Cys Tyr Ser Val Ala Ser Pro Ser Ser Phe Glu Asn Val
                                                                            288
acc tcg aaa tgg tat ccg gag ata aag cac cac tgt ccc gat gcg ccc
                                                                            336
Thr Ser Lys Trp Tyr Pro Glu Ile Lys His His Cys Pro Asp Ala Pro
                                  105
            100
                                                        110
atc att cta gtt ggc acc aaa atc gat ttg cgc gaa gat cga gag aca
                                                                            384
Ile Ile Leu Val Gly Thr Lys Ile Asp Leu Arg Glu Asp Arg Glu Thr
                              120
                                                   125
etc age gge etg gea gag eag gga etg aeg eeg etg aag ege gag eag
                                                                            432
Leu Ser Gly Leu Ala Glu Gln Gly Leu Thr Pro Leu Lys Arg Glu Gln
ggc cag aag ctg gca aac aag ata cgc gct gtg aaa tac atg gag tgc
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Gly Gln Lys Leu Ala Asn Lys Ile Arg Ala Val Lys Tyr Met Glu Cys
                     150
tee gee ttg acg cag ege ggt ete aag eeg gtg tte gag gaa geg gtg
                                                                           528
Ser Ala Leu Thr Gln Arg Gly Leu Lys Pro Val Phe Glu Glu Ala Val
                 165
                                      170
cgc gcg gtg ctc aga cca gag ccg cta aag cga cgc cag cga aag tgt
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tta ata atg taa
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Leu Ile Met
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225/291 135 140 egt gac atg gca aac egt atc tee gee tae geg tae atg gaa tge tet 480 Arg Asp Met Ala Asn Arg Ile Ser Ala Tyr Ala Tyr Met Glu Cys Ser 145 150 155 gca aaa acg aaa gat ggc gtg agg gaa gtg ttt gag ctg gct aca cgg 528 Ala Lys Thr Lys Asp Gly Val Arg Glu Val Phe Glu Leu Ala Thr Arg 165 170 gca gcc ctg caa gct agg cgt ggc aag aag aaa cca cgt tgc ctt ctc 576 Ala Ala Leu Gln Ala Arg Arg Gly Lys Lys Lys Pro Arg Cys Leu Leu 185 190 atc taa 582 Ile <210> 302 <211> 193 <212> PRT <213> Xenopus laevis <400> 302 Met Ala Ala Ile Arg Lys Leu Val Ile Val Gly Asp Gly Ala Cys Gly Lys Thr Cys Leu Leu Ile Val Phe Ser Lys Asp Gln Phe Pro Glu Val Tyr Val Pro Thr Val Phe Glu Asn Tyr Val Ala Asp Ile Glu Val Asp Gly Lys Gln Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Thr Asp Val Ile 75 Leu Met Cys Phe Ser Ile Asp Ser Pro Asp Ser Leu Glu Asn Ile Pro 90 Glu Lys Trp Thr Pro Glu Val Lys His Phe Cys Pro Asn Val Pro Ile 105 Ile Leu Val Gly Asn Lys Lys Asp Leu Arg Asn Asp Glu His Thr Arg 120 Arg Glu Leu Thr Lys Met Lys Gln Glu Pro Val Lys Pro Glu Glu Gly . 130 135 140 Arg Asp Met Ala Asn Arg Ile Ser Ala Tyr Ala Tyr Met Glu Cys Ser 150 Ala Lys Thr Lys Asp Gly Val Arg Glu Val Phe Glu Leu Ala Thr Arg 170 Ala Ala Leu Gln Ala Arg Arg Gly Lys Lys Lys Pro Arg Cys Leu Leu 185 190 Ile <210> 303 <211> 591 <212> DNA <213> Physcomitrella patens <220> <221> CDS -<222> (1)..(591) atg age aet tea egg ttt ate aag tge gtg aet gtt gga gat gga get 48 Met Ser Thr Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala 10 gtc ggg aag acg tgc atg ctt att tca tac acc agc aac aca ttt cct 96 Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Ser Asn Thr Phe Pro act gat tac gtt cct acc gtg ttt gac aac ttc agc gca aat gta gtg 144 Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val Val

gtc gat gga aat acc gtc aac ctc ggg tta tgg gat aca gca ggt caa

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Glu 65	Asp	Tyr	aac Asn	Arg	Leu 70	Arg	Pro	Leu	Ser	Tyr 75	Arg	Gly	Ala	Asp	Val 80	240
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ser	Lys	Lys	tgg Trp 100	Ile	Pro	Glu	Leu	Arg 105	His	Tyr	Ala	Pro	Ser 110	Val	Pro	336
atc Ile	att Ile	ctc Leu 115	gtc Val	gga Gly	aca Thr	aaa Lys	ctt Leu 120	gat Asp	ctt Leu	cgc Arg	gat Asp	gac Asp 125	aaa Lys	caa Gln	ttc Phe	384
ttt Phe	gct Ala 130	gat Asp	cat His	cct Pro	gga Gly	gcg Ala 135	gct Ala	cca Pro	ata Ile	act Thr	act Thr 140	tct Ser	caa Gln	gjà aaa	gag Glu	432
gag Glu 145	ctc Leu	agg Arg	aag Lys	tċg Ser	att Ile 150	Gly	gcg Ala	gcc Ala	tcg Ser	tac Tyr 155	ata Ile	gag Glu	tgc Cys	agc Ser	tca Ser 160	480
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gtt Val	ctc Leu	caa Gln	cca Pro 180	Pro	aag Lys	cag Gln	aag Lys	aag Lys 185	aag Lys	aag Lys	aaa Lys	aaa Lys	caa Gln 190	aag Lys	aat Asn	576
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<213> Physcomitrella patens

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<210> 305

<211> 841

<212> DNA

<213> Schistosoma mansoni

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			tgc Cys															96
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	atc Ile	gaa Glu	gtt Val	gat Asp 50	aac Asn	aga Arg	caa Gln	gtt Val	gaa Glu 55	tta Leu	gct Ala	ctc Leu	tgg Trp	gac Asp 60	act Thr	gct Ala		192
			gaa Glu 65															240
			gtt Val															288
			gag Glu															336
			att Ile						ГЛS									384
			aag Lys															432
			ggt Gly 145															480
			tca Ser														•	528
			cga Arg															576
	gat Asp			tgat	ctcc	eac t	gtto	ctcta	a at	tgto	ctaga	ttt	gati	tttc	cggt	ctcc	ga	635
	aaca	taca	att c	ccct	ccta	ıa tt	ctto	ctca	gga	icctt	aaa	ttgo	tact	ttc t	tatco	gctg	C	695
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	t <b>t</b> tg	ccat	tt a	ittt	tgcc	t to	gtac	taaa	ata	raggo	atg	ccto	atgt	taa d	cttat	attt	a	815
	ttga	.gaat	aa a	ıttac	tata	a to	agto	:	•			٠.						841

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<211> 193 <212> PRT

<213> Schistosoma mansoni

<400> 306

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35 Val Asp Asn 50	Arg	Gln '				Ala	Leu	Trp	Asp 60		Ala	Gly	Gln	
Glu Asp Tyr	Asp .		Leu i 70	Arg	Pro	Leu	Ser	Tyr 75	Pro	Asp	Thr	Asp	Val 80	
Val Leu Leu		Tyr :	Ser	Ile	qaA	Ser	Pro 90	qeA	Ser	Phe	Ala	Asn 95	Ile	
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Ile Val Lev 115	;				120					125				
Lys Asn Glu 130				135					140					
Gly Lys Glr			150					155					160	 
Ser Ala Lys		165					170					175		
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Ile														
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<211> 576 <212> DNA	_	_												
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Met Gln Th		5					10					15		96
acc tgt ct Thr Cys Le	tta Leu 20	Ile	ser	tac Tyr	aca Thr	aca Thr 25	aat Asn	aaa Lys	Phe	Pro	Ser 30	Glu	Tyr	96
gta cca ac Val Pro Th	a att	ttt	gat	aac Asn	tat Tvr	gct	gta Val	aca Thr	gtg Val	atg Met	att	gga Gly	gga Gly	144
gag cct ta					40					45				192
Glu Pro Ty 50	r Thr	Leu	Gly	Leu 55	Phe	Asp	Thr	Ala	Gly 60	Gln	Glu	Asp	Tyr	
gat aga tt Asp Arg Le	a cga u Arq	ccc Pro	ctc Leu	agc	tat Tyr	cca Pro	cag Gln	aca Thr	gat Asp	gta Val	ttt Phe	ctg Leu	gtc Val	240
65 tat ttt ta	a orto	gta	70 tct	cat	tct	tca	ttt	75 gaa	aat	gtg	aaa	gaa	aag	288
Cys Phe Se	r Val	Val 85	Ser	Pro	Ser	Ser	Phe 90	Glu	Asn	Val	Lys	95	Lys	
tgg gta cc Trp Val Pr	t gaa o Glu	att Ile	act Thr	cac His	cat His	tgt Cys	cca Pro	aag Lys	act Thr	ect	Phe	Lev	ctt Leu	336
att aga ac	100 c caa	att	gat	cta	aqa	105 gat	gat	ccc	tca	aca	110 att	gaa	aaa	384
Val Gly Th	r Gln 5	Ile	Asp	Leu	Arg 120	Asp	) Asp	Pro	Ser	125	ITE	GIU	гтув	
ctt gcc aa Leu Ala Ly	g aac s Asn	aag Lys	cag Gln	Lys	Pro	ata Ile	act Thr	CCa Pro	Glu	Thr	gct	gaa Glu	aaa Lys	432
130 cta acc co	d dac	ctq	aaq	135 gct	gtt	aaa	ı tat	gtg	140 gaa	. tgc	tct	: gcg	ctt	480
Leu Ala Ar 145	g Asp	Leu	Lys 150	Ala	. Val	. Lys	Tyr	Val 155	Glu 5	Cys	Ser	. Ale	160	
acg cag aa Thr Gln Ly	a ggc s Gly	cta Leu	aag Lys	aat Asn	gta Val	ttt. Phe	e Asp	Gli	g gcg	ata	tto Lev	ı Ala	a Ala	528
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576

185

Leu Glu Pro Pro Glu Pro Lys Lys Thr Arg Arg Cys Val Leu Leu

229/291

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tttg	rttt	ca c	tatt	tagt	t at	tgta	.acgt	tct	agtt	tga	aaat	ccat	tt c	tata	agat	539
atg Met 1	aca Thr	ccc Pro	aac Asn	ggc Gly	agt Ser	agg Arg	aga Arg	cat His	tcg Ser	gcg Ala	tac Tyr	atg Met	Gly aaa	tcg Ser 15	ccc Pro	587
aga	agc Ser	cag Gln	cat His 20	agt Ser	tcc Ser	aca Thr	atg Met	gaa Glu 25	aca Thr	ggt Gly	tac Tyr	aat Asn	cct Pro 30	tac Tyr	gaa Glu	635
gca Ala	gta Val	cag Gln 35	aaq	aaa Lys	cag Gln	gaa Glu	tta Leu 40	tac	caa Gln	aat Asn	aac Asn	aac Asn 45	ggc	aat Asn	tca Ser	683
cca Pro	acc Thr 50	atc	atc Ile	att Ile	gaa Glu	gaa Glu 55	gat	cca Pro	tac Tyr	atc Ile	cca Pro 60	aat Asn	tat Tyr	aaa Lys	gag Glu	7.31
Leu 65	tct Ser	Leu	Ala	Asn	Lys 70	aaa Lys	Thr	Asn	tat Tyr	Asn 75	Met	Lys	Ile	Val	Val 80	779
atc	ggt Gly	gac Asp	ggt Gly	999 Gly 85	tgt Cys	ggt Gly	aag Lys	acg Thr	tgt Cys 90	tta Leu	tta Leu	tta Leu	gca Ala	tac Tyr 95	aca Thr	827
caa Gln	aac Asn	aaa Lys	ttt Phe 100	cct Pro	tca Ser	atc Ile	tat Tyr	gtt Val 105	ccc Pro	aca Thr	gtt Val	ttt Phe	gag Glu 110	aat Asn	tat Tyr	875
gtg Val	acg Thr	gca Ala 115	gta	cag Gln	tcg Ser	cct Pro	aat Asn 120	ggt Gly	aaa Lys	acc Thr	gtg Val	gaa Glu 125	ttg Leu	gct Ala	ctc Leu	923
Trp	Asp	Thr	Ala	Gly	Gln	Glu 135	Glu	Tyr	gat Asp	Arg	Leu 140	Arg	Pro	Leu	ser	971 ·
Tyr 145	Pro	Asp	Val	Asp	Ile 150	Leu	Leu	Val	tgt Cys	Phe 155	Ala	Val	Asp	Asn	G1u 160	1019
Val	Ser	Leu	Glu	Asn 165	Val	Lys	Asp	Met	tgg Trp 170	Phe	Pro	GIU	vaı	175	HIS	1067
Tyr	Cys	Pro	Gly 180	Ile	Pro	Ile	Ile	Leu 185	gtt Val	Gly	Thr	Lys	Ser 190	Asp	Leu	1115
Leu	Ser	Asp	Met	Asn	His	Asp	Ala 200	Ser	ata Ile	Arg	Val	Ala 205	Lys	Glu	Ile	1163
Gly	Ala 210	Ile	Gly	Leu	Ile	Phe 215	Thr	Ser	gcc Ala	Lys	Thr 220	Met	Phe	Asn	Val	1211
Arg	Thr	Val	Phe	Asn	Phe 230	Ala	Leu	Asn	cat His	Phe 235	Gln	Arg	Asn	Met	G1u 240	1259
Leu	Gln	Glu	Gln	Tyr 245	Glu	Lys	Thr	Leu	ggt Gly 250	Ser	Arg	гуs	Arg	255	ser	1307
Arg	Val	Leu	Gly 260	Gly	Ser	Asn	Gly	Gly 265		Gly	Asn	His	Ser 270	Arg	HIS	1355 1403
His	Ser	Arg 275	Asn	Tyr	Ser	Asn	Val 280	Ser		Asr	ı Arg	Arg 285	Gly	His	Leu	
Lys	290	Thr	Ser	Туг	: Asp	Ser 295	Thr	Ala	Leu	Lev	300 300	Gln	Pro	Leu		145
Glu 305	Asp	Thr	Tyr	· Val	L Lys 310	Asn )	Pro	туг	Gly	Asr 315	ı Phe	Gly	Tyr	: Lys	gca Ala 320	1499
aat	gtt	gaa	ı agt	CCS	, tat	aat	: cag	gat	: gag	ttt	gca	. ctt	aca	aga	gaa	154

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231/291 Asn Val Glu Ser Pro Tyr Asn Gln Asp Glu Phe Ala Phe Thr Arg Glu 330 aga aag aag aaa aag tgt gta ata ttg tagatacctc tttgattagg 1597 Arg Lys Lys Lys Lys Cys Val Ile Leu tecataataa tatattaaag ttetgeatat gacaagaaat egttttgtag aaageacatg 1657 aaatcatqtc acaattqcat qqctaqttta Caggtctctg qatttcgaat tggatgaaag 1717 tataattata aaaccaatta qtgtctggga atactacata actgtctact gagatttcct 1777 atagtgagat atctaactgg tcaaagtgta gtacttttga agtgatattg ggttacttgc 1837 tgtatatatc gtcaatgttc cgtttatcct tcttatccga gactagtata gcaattatta 1897 tcattaatcc ttaacaaatq aacaggetcc agcttgtcga aaaaacactg ggcacttcat

2011

<210> 310 <211> 346 <212> PRT

<213> Candida albicans

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cattttgtag tggtaaatct ttatattggt ttccaatatt atagatcctc taga

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232/291	
His Ser Arg Asn Tyr Ser Asn Val Ser Asn Asn Arg Arg Gly His Leu 275 280 285	
Lys Asn Thr Ser Tyr Asp Ser Thr Ala Leu Leu Asp Gln Pro Leu Thr 290 295 300	
Glu Asp Thr Tyr Val Lys Asn Pro Tyr Gly Asn Phe Gly Tyr Lys Ala	
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325 330 335	
Arg Lys Lys Lys Lys Cys Val Ile Leu 340 345	
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ttttttttt taatttttt tgttaaaaaa atg agt gct tcg agg ttc ata aaa	114
Met Ser Ala Ser Arg Phe Ile Lys 1 5	
tgt gtt aca gtt ggt gat ggt gcc gtt ggt aaa act tgc ttg ttg att	162
Cys Val Thr Val Gly Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile 10 15 20	
tot tac acc age aac acc ttt cot acg gac tac gtg coc act gtt ttt	210
Ser Tyr Thr Ser Asn Thr Phe Pro Thr Asp Tyr Val Pro Thr Val Phe 25 30 35 40	
gac aat tto agt goo aat gto gto gtt aac ggg goo aca gtt aat ctg	258
Asp Asn Phe Ser Ala Asn Val Val Asn Gly Ala Thr Val Asn Leu	
gga tta tgg gat act gca gga caa gag gat tat aac aga tta aga cct	306
Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro	
ttg agt tat cgt gga gca gat gtt ttt att ctc gct ttc tcc ctt att	354
Leu Ser Tyr Arg Gly Ala Asp Val Phe Ile Leu Ala Phe Ser Leu Ile	
age aag get agt tat gaa aat gtt tet aag aag tgg att eet gag ttg	402
Ser Lys Ala Ser Tyr Glu Asn Val Ser Lys Lys Trp Ile Pro Glu Leu	
aag cat tat get eet ggt gte eee att gtt ett gtt gga aca aag ete	450
Lys His Tyr Ala Pro Gly Val Pro Ile Val Leu Val Gly Thr Lys Leu	
105 110 115 120 gat ctt cgg gat gac aag cag ttt ttt atc gac cac cct ggt gca gtt	498
Asp Leu Arg Asp Asp Lys Gln Phe Phe Ile Asp His Pro Gly Ala Val	
125 130 135 cca atc act aca gct cag gga gag gaa tta agg aaa ctg att ggg gct	546
Pro Ile Thr Thr Ala Gln Gly Glu Leu Arg Lys Leu Ile Gly Ala	
140 145 150 cct gct tac atc gaa tgc agt tca aaa aca cag cag aat gtc aag gca	594
Pro Ala Tyr Ile Glu Cys Ser Ser Lys Thr Gln Gln Asn Val Lys Ala	
155 160 165 gtt ttt gat gca gcc att aag gtc gtg ctt caa cca cca aag aca aag	642
Val Phe Asp Ala Ala Ile Lys Val Val Leu Gln Pro Pro Lys Thr Lys	
170 175 180	691
aaa aag aag tca aag gca cag aag gct tgc tcc ata ttg taattgtgta Lys Lys Lys Ser Lys Ala Gln Lys Ala Cys Ser Ile Leu	<b>421</b>
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135

ctg gcc aag gag att gac tet gtg aag tac ctg gag tgc tca gcc ctc

Leu Ala Lys Glu Ile Asp Ser Val Lys Tyr Leu Glu Cys Ser Ala Leu

140

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234/291 155 145 ace cag aga gge etg aag ace gte ttt gae gag gee ate egt gee gte 528 Thr Gln Arg Gly Leu Lys Thr Val Phe Asp Glu Ala Ile Arg Ala Val 170 175 165 ctg tgc cct cag ccc acg cgg cca cag aag cgc gcc tgc agc ctc ctc 576 Leu Cys Pro Gln Pro Thr Arg Pro Gln Lys Arg Ala Cys Ser Leu Leu 190 581 ta taq

<210> 314 <211> 192 <212> PRT <213> Cavia porcellus

~400× 314 ···· Met Gln Ala Ile Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys 10 Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Ala Phe Pro Gly Glu Tyr 30 25 20 Ile Pro Thr Val Phe Asp Asn Tyr Ser Ala Asn Val Met Val Asp Ser 40 Lys Pro Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr 55 Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Ile 75 Cys Phe Ser Leu Val Ser Pro Ala Ser Tyr Glu Asn Val His Ala Asn 85 Trp Tyr Pro Lys Val Arg His His Cys Pro Ser Thr Pro Ile Ile Leu 1.05 Leu Gly Thr Lys Leu Asp Leu Arg Asp Asp Lys Glu Thr Ile Glu:Lys 125 120 115 Leu Lys Glu Lys Lys Leu Ala Pro Ile Thr Tyr Pro Gln Gly Leu Ala 140 135 130 Leu Ala Lys Glu Ile Asp Ser Val Lys Tyr Leu Glu Cys Ser Ala Leu 155 150 Thr Gln Arg Gly Leu Lys Thr Val Phe Asp Glu Ala Ile Arg Ala Val 175 170 Leu Cys Pro Gln Pro Thr Arg Pro Gln Lys Arg Ala Cys Ser Leu Leu 185

<210> 315 <211> 982 <212> DNA <213> Lotus japonicus

<220> <221> CDS <222> (113)..(703)

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								<b>20012</b> .	<b>,</b>								
Gly	agc Ser	aca Thr	gtt Val	aac Asn 55	ctg Leu	gga Gly	tta Leu	tgg Trp	gac Asp 60	act Thr	gct Ala	gga Gly	cag Gln	gag Glu 65	gat Asp		310
Tyr	Asn	Arg	Leu 70	Arg	Pro	Leu	Ser	Tyr 75	Arg	Gly		Asp	Val 80	Phe	Leu		358
ctġ Leu	gct Ala	ttt Phe 85	tcc Ser	ctc Leu	ctt Leu	agc Ser	aga Arg 90	gcc Ala	agc Ser	tat Tyr	gaa Glu	aat Asn 95	atc Ile	tcc Ser	aaa Lys		406
Lys	Trp 100	Ile	Pro	Glu	Leu	Arg 105	His	Tyr	Ala	Pro	act Thr 110	Val	Pro	Ile	Val		454
Leu 115	Val	Gly	Thr	Lys	Leu 120	Asp	Leu	Arg	Glu	Asp 125	agg Arg	Gln	Tyr	Leu	Ile 130		502
Asp	His	Pro	Gly	Ala 135	Thr	Pro	Ile	Thr	Thr 140	Ala	cag Gln	Gly	Glu	Glu 145	Leu	•	550
Lys	Lys	Ala	Ile 150	Gly	Ala	Ala	Val	Tyr 155	Leu	Glu	tgc Cys	Ser	Ser 160	Lys	Thr		598
Gln	Gln	Asn 165	Val <sub>.</sub>	ГÀв	Ala	Val	Phe 170	Asp	Ala	Ala	atc Ile	Lys 175	Val	Val	Leu		646
Gln	Pro 180	Pro	Lys	Pro	Lys	Lys 185	Lys	Arg	ГЛЗ	Lys	acc Thr 190	Arg	Pro	Cys	Val		694
ttc Phe 195	ctt Leu	taat	tgat	gt t	cato	tttg	ja tt	cgca	atct	gta	ıgcat	tcg	ggac	cttc	:tt		750 ·
:.															ttaca		810
										•					itttca		870
															rataag	<b>Γ</b> .	930
aaat	aata	gc a	ttca	tagt	g ac	tttt	ttta	. tta	iaaaa	aaa	aaaa	.aaaa	aa a	.a.			982

<210> 316

<211> 196

<212> PRT

<213> Lotus japonicus

<400> 316

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Glu Leu Lys Lys Ala Ile Gly Ala Ala Val Tyr Leu Glu Cys Ser Ser
                                        155
                    150
Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys Val
                                                        175
                                  170
                165
Val Leu Gln Pro Pro Lys Pro Lys Lys Lys Arg Lys Lys Thr Arg Pro
                                185
Cys Val Phe Leu
        195
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<211> 659
<212> DNA
<213> Dictyostelium discoideum
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<221> CDS
<222> (22)..(609)
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                        1
gat ggt gct gtt ggt aaa act tgt tta tta att tct tat aca tca aat
                                                                       99
Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser Asn
                15
tct ttc cca aca gaa tac gtt cca act gta ttt gat aac tat tca gca
                                                                       147
Ser Phe Pro Thr Glu Tyr Val Pro Thr Val Phe Asp Asn Tyr Ser Ala
                                35
                                                                       195
aat gtt atg gta gat aat aaa act gtt tca tta ggt ctt tgg gat act
Asn Val Met Val Asp Asn Lys Thr Val Ser Leu Gly Leu Trp Asp Thr
                            50
                                                55
        45
gct ggt caa gag gat tat gat cgt tta: aga cca ctt tca tac cca caa
                                                                       243
Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln
                        65
                                                                       291
acc gat gtt ttt ctt att tgt ttc gct att ata agt caa act tca tat
Thr Asp Val Phe Leu Ile Cys Phe Ala Ile Ile Ser Gln Thr Ser Tyr
                                         85
                    80
aca aat gta aaa tct aaa tgg tgg cct gaa gtc aca cat cat tgt cca
                                                                       339
Thr Asn Val Lys Ser Lys Trp Trp Pro Glu Val Thr His His Cys Pro
                                     100
aac tgc aca att att tta gtt ggt aca aaa tgt gat tta aga gaa gac
                                                                       387
Asn Cys Thr Ile Ile Leu Val Gly Thr Lys Cys Asp Leu Arg Glu Asp
                                                 120
             110
                                 115
 aaa gaa agt tta gaa aaa ctc aga gaa aaa cat caa caa cca ctc acc
                                                                       435
Lys Glu Ser Leu Glu Lys Leu Arg Glu Lys His Gln Gln Pro Leu Thr
                                                135 ·
                            130
 ttc caa caa ggt gaa caa atg gca aaa gaa att aaa gcc ttt tgt tat
                                                                       483
 Phe Gln Gln Gly Glu Gln Met Ala Lys Glu Ile Lys Ala Phe Cys Tyr
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                         145
 atg gaa tgt tcc gct tta act caa aaa ggt ctc aaa caa gtt ttc gac
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 Met Glu Cys Ser Ala Leu Thr Gln Lys Gly Leu Lys Gln Val Phe Asp
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                     160
 gaa gct att aaa gct gtt att ttc cca gat aga gat aag gcc aca aac
                                                                       579
 Glu Ala Ile Lys Ala Val Ile Phe Pro Asp Arg Asp Lys Ala Thr Asn
                                    180
                 175
 aaa aag aat tca aaa tgt tca att tta taaaaacata tcaaaatatc
                                                                       626
 Lys Lys Asn Ser Lys Cys Ser Ile Leu
             190
                                                                       659
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<sup>&</sup>lt;210> 318 <211> 195

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Dictyostelium discoideum

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Val Pro Thr Val Phe Asp Asn Tyr Ser Ala Asn Val Met Val Asp Asn
Lys Thr Val Ser Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr
Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Ile
                      70
Cys Phe Ala Ile Ile Ser Gln Thr Ser Tyr Thr Asn Val Lys Ser Lys
Trp Trp Pro Glu Val Thr His His Cys Pro Asn Cys Thr Ile Ile Leu
             100
                                   105
Val Gly Thr Lys Cys Asp Leu Arg Glu Asp Lys Glu Ser Leu Glu Lys
                              120
                                                    125
Leu Arg Glu Lys His Gln Gln Pro Leu Thr Phe Gln Gln Gly Glu Gln
                          135
Met Ala Lys Glu Ile Lys Ala Phe Cys Tyr Met Glu Cys Ser Ala Leu
                      150
                                           155
Thr Gln Lys Gly Leu Lys Gln Val Phe Asp Glu Ala Ile Lys Ala Val
                                       170
                 165
Ile Phe Pro Asp Arg Asp Lys Ala Thr Asn Lys Lys Asn Ser Lys Cys
                                   185
Ser Ile Leu
        195
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57
                                                      Met Ser Ala Ala
gaa gtt att aaa tta gtc gtt att ggt gat ggt gct gta ggt aaa act
Glu Val Ile Lys Leu Val Val Ile Gly Asp Gly Ala Val Gly Lys Thr
                                                                           105
tgt tta ttg att agt tat gca aac aat cgt ttc cca gaa gat tat att
                                                                           153
Cys Leu Leu Ile Ser Tyr Ala Asn Asn Arg Phe Pro Glu Asp Tyr Ile
                 25
                                      30
cca act gta ttc gat aat tat gtt gta aat ctt aca gca ggt gat aga
Pro Thr Val Phe Asp Asn Tyr Val Val Asn Leu Thr Ala Gly Asp Arg
                                                                           201
             40
                                  45
                                                        50
aac ata gaa ctc gga ctt tgg gat act gca ggt caa gaa gag tac gat
                                                                           249
Asn Ile Glu Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Glu Tyr Asp
                              60
aaa tta aga cca tta agt tat gca aat gca aat gta ttt tta att tgc
                                                                           297
Lys Leu Arg Pro Leu Ser Tyr Ala Asn Ala Asn Val Phe Leu Ile Cys
ttc tca att acc aat cca gtt tca ttt gaa aat gtt tac aca aaa tgg
                                                                           345
Phe Ser Ile Thr Asn Pro Val Ser Phe Glu Asn Val Tyr Thr Lys Trp
                     90
                                           95
tac cca gaa gtt atg cat ttt tgc cca gaa gtt cca caa att tta gtt Tyr Pro Glu Val Met His Phe Cys Pro Glu Val Pro Gln Ile Leu Val
                                                                           393
                 105
                                      110
ggt act aaa tta gat aca cgt gac gat aga ggt gtt tta gat aaa ctt
                                                                           441
Gly Thr Lys Leu Asp Thr Arg Asp Asp Arg Gly Val Leu Asp Lys Leu
            120
                                  125
caa caa act ggt cat aaa cca att aca acc gaa caa ggt aac gat tta
                                                                           489
Gln Gln Thr Gly His Lys Pro Ile Thr Thr Glu Gln Gly Asn Asp Leu
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WO 2005/014828 PCT/EP2004/008136

238/291 gcc aga aga att aaa gcc att aaa tat atg gaa tgt tct gcc aaa acc 537 Ala Arg Arg Ile Lys Ala Ile Lys Tyr Met Glu Cys Ser Ala Lys Thr 160 150 155 tca caa aat ctc aaa caa gtc ttt gat gaa gcc att aaa tct gtt ttg 585 Ser Gln Asn Leu Lys Gln Val Phe Asp Glu Ala Ile Lys Ser Val Leu 175 170 ttt atc aaa aaa aag aaa tcc aag tgt att gtt atg taacccgctc 631 Phe Ile Lys Lys Lys Ser Lys Cys Ile Val Met 185

634

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65					Asp 70					75					80		
Asp	Val	Phe	Ile	Ile 85	tgt Cys	Tyr	Ser	Val	Val 90	Lys	Arg	Asp	Ser	Leu 95	Asp		288
Asn	Ile	ГÀЗ	Tyr	Lys	Trp	Leu	Pro	Glu 105	Ile	Asn	.Gln	Thr	Asn 110	Gln			336
aca Thr	cca Pro	att Ile 115	att Ile	tta Leu	gtt Val	ggt Gly	aca Thr 120	aag Lys	act Thr	gat Asp	tta Leu	agg Arg 125	gag Glu	gac Asp	aaa Lys	· .	384
aaa Lys	aca Thr 130	tta Leu	tca Ser	caa Gln	tta Leu	caa Gln 135	gaa Glu	tca Ser	Lys Lys	caa Gln	gaa Glu 140	cca Pro	gtt Val	tca Ser	aga Arg		432
gat Asp 145	gaa Glu	ggt Gly	gta Val	gca Ala	tta Leu 150	gca Ala	aaa Lys	gag Glu	ata Ile	ggt Gly 155	gca Ala	gta Val	caa Gln	ttt Phe	ttc Phe 160		480
gaa Glu	tgt Cys	tct Ser	gca Ala	ttg Leu 165	aca Thr	ggt Gly	aat Asn	ggt Gly	gta Val 170	aat Asn	gat Asp	att	ttc Phe	gct Ala 175	gct Ala		528
gca Ala	att Ile	aaa Lys	gca Ala 180	gct Ala	ttt Phe	aat Asn	aaa Lys	cct Pro 185	gct Ala	gta Val	act Thr	tca Ser	cca Pro 190	act Thr	tcg Ser		576
		_			tct Ser												624
					act Thr												672
gct Ala 225	gct Ala	tca Ser	act Thr	gca Ala	aaa Lys 230	cca. Pro	gca Ala	ggt Gly	gaa Glu	aag Lys 235	aaa Lys	tta Leu	agt Ser	tgg Trp	ggt Gly 240		720
					gat Asp					aaa							765

<210> 322

<211> 254

<212> PRT

<213> Dictyostelium discoideum

<400> 322

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200

205

240/291

195

Lys Thr Thr Thr Thr Thr Thr Ser Ser Ser Ser Ser Pro Pro 215 220 Ala Ala Ser Thr Ala Lys Pro Ala Gly Glu Lys Lys Leu Ser Trp Gly 230 235 Leu Phe Arg Lys Lys Asp Lys Asp Glu Lys Lys Pro Ala Lys 245 <210> 323 <211> 672 <212> DNA <213> Dictyostelium discoideum <220> <221> CDS <222> (1)..(672) atg tca gaa gat caa ggt tca gga gca aca aga gtt aaa tta gta gtt Met Ser Glu Asp Gln Gly Ser Gly Ala Thr Arg Val Lys Leu Val Val 10 gtc ggt gat ggt gct gtt ggt aaa aca tgt ctt tta att tgt tat gca 96 Val Gly Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile Cys Tyr Ala 30 25 caa aat gat ttt cca gta gat tat gta cca act gtt ttt gaa aat tat 144 Gln Asn Asp Phe Pro Val Asp Tyr Val Pro Thr Val Phe Glu Asn Tyr 45 40 35 aca gca acc aga aag aga gga aat gaa gat att aaa gta cat tta tgg 192 Thr Ala Thr Arg Lys Arg Gly Asn Glu Asp Ile Lys Val His Leu Trp 60 **55** . gat act gca ggc caa gaa gaa tat gat cgt tta cgt cca tta tca tac 240 Asp Thr Ala Gly Gln Glu Glu Tyr Asp Arg Leu Arg Pro Leu Ser Tyr 75 70 cca ggc gct gat gtt gtt ctc ctt tgt ttc agc aca atc agt caa tca 288 Pro Gly Ala Asp Val Val Leu Leu Cys Phe Ser Thr Ile Ser Gln Ser 85 tca tat gaa gcc att aga gat aaa tgg gca cca gaa gtt aat cac tat 336 Ser Tyr Glu Ala Ile Arg Asp Lys Trp Ala Pro Glu Val Asn His Tyr 105 384 atc cca gat gta cca tca att tta gtt ggt act aaa atc gat tta cgt Ile Pro Asp Val Pro Ser Ile Leu Val Gly Thr Lys Ile Asp Leu Arg 125 120 115 gaa caa caa cac cca gat cca aac tct ggt aaa ttc gaa cca atc act 432 Glu Gln Gln His Pro Asp Pro Asn Ser Gly Lys Phe Glu Pro Ile Thr 135 130 gcc gat atg ggt att tca atg caa aaa caa att aaa gcc aag aaa tat 480 Ala Asp Met Gly Ile Ser Met Gln Lys Gln Ile Lys Ala Lys Lys Tyr 150 tta gaa gtc tct gca aag act cgt caa ggt tta gaa gaa gtt ttc agt 528 Leu Glu Val Ser Ala Lys Thr Arg Gln Gly Leu Glu Glu Val Phe Ser 170 165 576 qct gcc att gaa atc gtt ctt gaa tca aga ggt atg gat aaa aag agt Ala Ala Ile Glu Ile Val Leu Glu Ser Arg Gly Met Asp Lys Lys Ser 185 190 180 caa gat ggt tct tca agt gca tct ggt gtt cca tca ggt gat aaa cca 624 Gln Asp Gly Ser Ser Ser Ala Ser Gly Val Pro Ser Gly Asp Lys Pro 200 205 aca aaa gga aaa gca ggt aaa aag aaa tct ggt tgt att ata ctt 669 Thr Lys Gly Lys Ala Gly Lys Lys Lys Ser Gly Cys Ile Ile Leu 672 taa

<210> 324 <211> 223 <212> PRT 241/291 <213> Dictyostelium discoideum

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							_	72,22	-		140					
Met	130 gct Ala	aag Lys	gag Glu	atg Met	Gly	135 gct Ala	gta Val	aaa Lys	tac Tyr	Leu	140 gag Glu	tgc Cys	ttg Leu	Ala	ctc Leu 160	480
145 aca Thr	agg Arg	cga Arg	ggc	Leu	150 aag Lys	aca Thr	gtg Val	ttt Phe	gac Asp 170	155 gaa Glu	gcg Ala	atc Ile	cga Arg	gct	gtc	528
ctc Leu	tgc Cys	cca Pro	cct Pro 180	165 ccc Pro	gtg Val	aag Lys	aag Lys	agg Arg 185	aag	aga Arg	aaa Lys	cys Cys	ctg Leu 190	cag	ttg Leu	576
tag			100					100								579
	)> 32 L> 19															 
<213		omo s	sapie	ens												
Met	0> 32 Gln	26 Ala	Ile	Lys	Gly	Val	Val	Val		Asp	Gly	Ala	Val	Gly 15	Lys	
1 Thr	Cys	Leu	Leu	Ile	Ser	Tyr	Thr		10 Asn	Ala	Phe	Pro	Gly 30		Asp	
Ile	Pro		20 Ala	Phe	Asp	Asn		25 Ser	Ala	Asn	Val	Met 45		Asp	Gly	
Lys		35 Val	Asn	Leu	Gly		40 Trp	Asn	Thr	Ala	Gly 60		Glu	Asp	Tyr	
	50 Arg	Leu	Arg	Pro	Leu 70	55 Ser	Tyr	Pro	Gln	Ala 75		Val	Phe	Leu	Ile 80	
65 Cys	Phe	Ser	Leu			Pro	Ala	Ser	Phe 90		Așn	Val	Leu	Ala 95		
Trp	Tyr	Pro	Glu 100	85 Val	Gln	His	His	Cys 105		Asn	Thr	Pro	Ile 110		Leu	
Val	Gly	Thr 115	Lys	Leu	Asp	Leu	Arg 120		Asp	Lys	qaA	Arg 125		Gln	Lys	
Leu	Lys 130	Glu	Lys	Lys	Leu	Thr 135		Ile	Thr	Tyr	Pro 140		Gly	Leu	Ala	
Met 145	Ala	Lys	Glu	Met	Gly 150	Ala	Val	Lys	Tyr	Leu 155	Glu	Сув	Leu	Ala	Leu 160	
Thr	Arg	Arg	Gly	Leu 165	Lys		Val	Phe	Asp 170	Glu	Ala	Ile	Arg	Ala 175	Val	
Leu	Cys	Pro	Pro 180			Lys	Lys	Arg 185		Arg	Lys	Сув	Leu 190	Gln	Leu	
<21 <21	0 > 3 1 > 5 2 > D 3 > D	94 NA	oste	lium	dis	coid	eum									
	1> C		(589	)												
<40 cat	Me	с са	a go n Al	a at a Il	t aa .e Ly 5	a tg s Cy	t gt s Va	a gt 1 Va	t gt	t gg 1 Gl	y As	t gg p Gl	rt go y Al	a gt a Va	t ggt l Gly	49
aaa Lys	aca Thr	tgt Cys	ctt Lev	tta Leu 20	att	tca Ser	tat Tyr	aca Thr	acc Thr	aat	gct	ttt Phe	cca Pro	gga Gly 30	gag Glu	97
tat Tyr	ato	cca Pro	aca Thr	gtt	ttt. Phe	gat Asp	aat Asn	tac Tyr 40	ago	gca	aat Asr	gta Val	a ato L Met	gtt	gat Asp	145
ggt	aaa Lys	cca Pro 50	att	aat Asr	cto Lev	gga Gly	tta Leu 55	tgo	gat Asp	aca Thi	gca Ala	ggt Gly 60	caa	ı gaa ı Glu	gat Asp	193

#### 243/291. tat gat cgt tta cgt cct tta tcc tat cct caa act gat gtt ttc tta Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu 70 75 att tgt ttt tca atc gtt tca cca gca tct ttt gag aat gta aat ggt 289 Ile Cys Phe Ser Ile Val Ser Pro Ala Ser Phe Glu Asn Val Asn Gly 85 . 90 95 aaa tgg cat cca gaa ata tgt cac cat gca cca aat gtt cga atc att 337 Lys Trp His Pro Glu Ile Cys His His Ala Pro Asn Val Arg Ile Ile 100 105 tta gtt ggt act aaa tta gat atg aga gat aga gat act caa gat 385 Leu Val Gly Thr Lys Leu Asp Met Arg Glu Asp Arg Asp Thr Gln Asp 120 125 aga tta aaa gag aaa aaa ctt tat cca gtt tcc tat gaa caa ggt ctt 433 Arg Leu Lys Glu Lys Lys Leu Tyr Pro Val Ser Tyr Glu Gln Gly Leu 130 135 140 tca aaa atg aaa gaa att aat gct gtc aaa tat ctt gaa tgt tca gct 481 Ser Lys Met Lys Glu Ile Asn Ala Val Lys Tyr Leu Glu Cys Ser Ala . 150 155 .... ctc aca caa aaa ggt ctt aaa act gtt ttt gat gaa gca att aga tct 529

170

185

577

594

Leu Thr Gln Lys Gly Leu Lys Thr Val Phe Asp Glu Ala Ile Arg Ser

gta att aat cca act ctt aag aaa aaa cca aaa tct tca aaa ggt tgt

Val Ile Asn Pro Thr Leu Lys Lys Lys Pro Lys Ser Ser Lys Gly Cys

<210> 328 <211> 194 <212> PRT

<213> Dictyostelium discoideum

att ata atg taaaaaaa

Ile Ile Met

165

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Ile Met

<sup>&</sup>lt;210> 329

<sup>&</sup>lt;211> 591

<sup>&</sup>lt;212> DNA

<sup>&</sup>lt;213> Dictyostelium discoideum

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Gly	Lys	Thr	Cys	Leu	Leu 20	Ile	Ser	Tyr	Thr.	Thr 25	Asn	gct Ala	Pne	Pro	30 GTA		97
mam.	tat Tyr	atc Ile	cca Pro	aca Thr 35	gtt Val	ttc Phe	gat Asp	aat Asn	tac Tyr 40	tca Ser	gct Ala	aat Asn	gtt Val	atg Met 45	gtt Val		145
gat Asp	ggt Gly	aaa Lys	cca Pro 50	att	aat Asn	ctt Leu	ggc Gly	ttg Leu 55	tgg Trp	gat Asp	act Thr	gct Ala	ggt Gly 60	caa Gln	gaa Glu	•	193
gat Asp	tat Tyr	gat Asp 65	cat	tta Leu	cgt Arg	cca Pro	ctt Leu 70	tca Ser	tat Tyr	cct Pro	caa Gln	act Thr 75	_gat Asp	gtt Val	ttc Phe		241
tta Leu	att Ile 80	tac	ttt Phe	tca Ser	att Ile	att Ile 85	tct	cca Pro	tca Ser	tca Ser	tat Tyr 90	gaa Glu	aat Asn	gtt Val	tca Ser		289
ggt Gly 95	aaa'	tgg Trp	gga Gly	cca Pro	gaa Glu 100	σta	ttt Phe	cat His	cat His	gct Ala 105	cca Pro	aat Asn	gtt Val	cca Pro	atc Ile 110		337
att	ttg Leu	gtt Val	ggt Gly	aca Thr 115	aaa	atg Met	gat Asp	atg Met	aga Arg 120	gaa Glu	gat Asp	aag Lys	gaa Glu	act Thr 125	caa Gln		385
gat Asp	aga Arg	tta Leu	aaa Lys 130	gaa	aag Lys	aaa Lys	ctt Leu	tat Tyr 135	Pro	gtt Val	tcc Ser	tat Tyr	gaa Glu 140	caa Gln	ggt Gly		433
ctt Leu	tta Leu	aaa Lys 145	atg Met	aaa Lys	gaa Glu	att Ile	aat Asn 150	gct Ala	ttc	aaa Lys	tat Tyr	ctt Leu 155	GIU	tgc Cys	tct Ser		481
gct Ala	ctc Leu 160	act Thr	caa	aaa Lys	ggt Gly	ctt Leu 165	aaa Lys	act	gtt Val	ttc Phe	gac Asp 170	gaa Glu	gct	att	aga Arg		529
Ser	gta Val	att	aat Asn	cca Pro	cca Pro 180	gtt Val	aaa	aaa Lys	tca Ser	aaa Lys 185	agt Ser	aaa	agt Ser	gga Gly	tgt Cys 190		577
	ato	ttg Leu		.aa	100												591

<210> 330 <211> 193

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<213> Dictyostelium discoideum

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135
     130
                                                140
 Lys Met Lys Glu Ile Asn Ala Phe Lys Tyr Leu Glu Cys Ser Ala Leu
                      150
                                            155
 Thr Gln Lys Gly Leu Lys Thr Val Phe Asp Glu Ala Ile Arg Ser Val
                  165
                                       170
 Ile Asn Pro Pro Val Lys Lys Ser Lys Ser Lys Ser Gly Cys Asn Ile
                                  185
 Leu
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Met Arg Pro Val Lys Leu Val Ile Val Gly
                                                                            51
 gat ggt gcc gtc ggt aaa act tgt atg tta att tca tat aca aca aat
                                                                            99
 Asp Gly Ala Val Gly Lys Thr Cys Met Leu Ile Ser Tyr Thr Thr Asn
                  15
                                       20
 gct ttc cca aat gaa tat att cca aca gtc ttt gaa aat tat aat tct
Ala Phe Pro Asn Glu Tyr Ile Pro Thr Val Phe Glu Asn Tyr Asn Ser
                                                                           . 147
                                   35
                                                        40
 tca ttg gtt gtt gat gat gtt aaa att aat ctt gga tta tgg gat act
                                                                            195
 Ser Leu Val Val Asp Asp Val Lys Ile Asn Leu Gly Leu Trp Asp Thr
                               50
                                                    55
 gct gga caa gaa gat tat gat aga tta aga cca tta tca tat cca tca
                                                                            243
 Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Ser
                          65
 act gat gta ttc ctt gtt tgt ttc tcc gtt att gct cca gct tca tat
                                                                            291
 Thr Asp Val Phe Leu Val Cys Phe Ser Val Ile Ala Pro Ala Ser Tyr
                      80
                                           85
                                                                 90
 gaa aat gtt gaa ggt aaa tgg aaa cca gaa att gat caa cac tgt cca
                                                                            339
 Glu Asn Val Glu Gly Lys Trp Lys Pro Glu Ile Asp Gln His Cys Pro
                                       100
 aat gta cca att att ctt gtt gga act aaa att gat att aga gat gat
                                                                            387
 Asn Val Pro Ile Ile Leu Val Gly Thr Lys Ile Asp Ile Arg Asp Asp
                                   115
                                                        120
 cca gaa caa gtt aaa cgt tta gct gaa aag aat att gtc cca att caa
                                                                            435
Pro Glu Gln Val Lys Arg Leu Ala Glu Lys Asn Ile Val Pro Ile Gln
         125
                               130
 ect cet caa gga gat gaa tta gca aag aaa att ggt gct gtt aaa tat
                                                                            483
 Pro Pro Gln Gly Asp Glu Leu Ala Lys Lys Ile Gly Ala Val Lys Tyr
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                                               150
att gaa tgt tct gct tta aca caa gcc aat ctt aaa ctt gtt ttt gaa
                                                                           531
 Ile Glu Cys Ser Ala Leu Thr Gln Ala Asn Leu Lys Leu Val Phe Glu
                      160
                                           165
gaa get gtt aga get gtt ett get aaa get get aaa gag eea aet gga
                                                                            579
Glu Ala Val Arg Ala Val Leu Ala Lys Ala Ala Lys Glu Pro Thr Gly
aag aaa gaa aaa gga ggt aag aaa gga tgc tca tta ttc taatttcact
                                                                            628
Lys Lys Glu Lys Gly Gly Lys Lys Gly Cys Ser Leu Phe
             190
                                  195
ttttagttga taaattgaag aagttgttat aaaagaaaat atatttgttt tttgtaaaaa
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aatagaaaat aaaagaagaa aaagattgat ttaaa
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<211> 199
<212> PRT
<213> Entamoeba histolytica
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Asp Arg Leu Arg Pro Leu Ser Tyr Pro Ser Thr Asp Val Phe Leu Val
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Cys Phe Ser Val Ile Ala Pro Ala Ser Tyr Glu Asn Val Glu Gly Lys
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Trp Lys Pro Glu Ile Asp Gln His Cys Pro Asn Val Pro Ile Ile Leu
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gat ggt gct tgt ggt aag act tgt tta tta att gtt ttt tca aaa ggt
                                                                       96
Asp Gly Ala Cys Gly Lys Thr Cys Leu Leu Ile Val Phe Ser Lys Gly
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act ttc cca gaa gtt tat gtc cca aca gtt ttt gaa aat tac gtt gct
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Thr Phe Pro Glu Val Tyr Val Pro Thr Val Phe Glu Asn Tyr Val Ala
gat gtt gaa gtt gat ggt aga aaa gtt gaa ttg gca tta tgg gat act
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Asp Val Glu Val Asp Gly Arg Lys Val Glu Leu Ala Leu Trp Asp Thr
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                     70
tct aat gtt att ttg att tgt ttt tca gtt gat tca cca gat tct tta
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Ser Asn Val Ile Leu Ile Cys Phe Ser Val Asp Ser Pro Asp Ser Leu
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Asp Asn Val Leu Glu Lys Trp Ile Ser Glu Val Leu His Phe Cys Gln
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 ggt gtt cca atc att tta gtt ggt tgt aaa tct gat tta aga gat gat
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Gly Val Pro Ile Ile Leu Val Gly Cys Lys Ser Asp Leu Arg Asp Asp
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 cct cat act att gaa gcc ttg aga caa caa caa caa caa cca gtc tca
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Pro His Thr Ile Glu Ala Leu Arg Gln Gln Gln Gln Pro Val Ser

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130		13	5			140				
act tct gaa	ggc caa				T2 2++					400
Thr Ser Glu	gge cae	Caa yu	1 372	Caa as	ja all	991	get g	ct gat	: tac	480
Thr Ser Glu	GIA GII		L ALA	GID AI			Ala A	la Asp	) Tyr	
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ttg gaa tgt	tct gct	aaa ac	c ggt	aga go	rt att	aga	gaa g	ta ttt	: gaa	528
Leu Glu Cys	Ser Ala	Livs Th	r ดีโซ	Arg Gl	v Val	Ara	Glu V	al Dho	. Glu	320
<b>4</b> -	165					AL 9	Gra v			
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gct gct act	aga gct	: tct tt	a aga	gtt aa	la gaa	aag .	aag g	aa aac	r aag	576
Ala Ala Thr	Arg Ala	Ser Lei	ı Ara	Val Ly	s Glu	Lvs	Tws G	lu Tare	Tare	7.7.
	180		5	185		_,_		_	, Lyb	•
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aag aaa tgt			ì							597
Lys Lys Cys	Val Val	. Leu								
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1				111.9	9 -173	Deu	var 1.		GIA	
				7.0			•	15		
Asp Gly Ala	Cys Gly	Lys Thr	Cys	Leu Le	u Ile	Val 1	Phe Se	er Lvs	Glv	
	20	•	-	25					<b>U</b> _,	
The Dhe Dee		·					3 (			•
Thr Phe Pro	GIU VAI	Tyr val	. Pro	Thr Va	I Phe	Glu 2	Asn Ty	r Val	Ala	
35			40				45			
Asp Val Glu	Wall Aco	Cl ** 3***		77-7 07						•
	var nsp	GIY ALG	пув	var Gr	u Leu	ATA 1	Leu Ti	rp Asp	Thr	
50		55				60 ·				
Ala Gly Gln	Glu Asp	Tyr Asr	Ara	Len Ar	T Pro	T.011 6	Ser Ta	m Dro	Acn .	•
65		70		204 11		Heu .	er ra	L PIO	Asp	
		70			75				80	
Ser Asn Val	Ile Leu	Ile Cys	Phe	Ser Va	l: Asp	Ser I	ero As	sp Ser	Leu	
•	85	•	•	90						
3 3 : TI- 3								95		
Asp Asn Val	ren ern	ras arb	Ile	ser GI	u Val	Leu I	lis Pl	le Cys	Gln	
	100			105	•		1.1	_		
Gly Val Pro		T.011 179 1	Glaz			3 T				
Gly Val Pro	TTE TTE	neu var		сув гу	s ser	Asp I	eu Ar	gAsp	Asp	
. 115			120				L25			
Pro His Thr	Ile Glu	Ala Leu	Ara	Gin Gi	n Gln	Gin G	in Dr	ro Wal	Cor	
130				<b>U</b>				. Vai	261	*
		135				140				
Thr Ser Glu	GIA GIU	Gln Val	Ala	Gln Ar	g Ile	Gly A	Ala Al	a Asp	Tyr	
145	•	150			155	_			160	•
Len Clu Cva	Cor Ala		~1	× 01.					100	
Leu Glu Cys		nas ruit	GTA	ALG GI	y var	Arg G	aru va	rr bue	GIU	
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Ala Ala Thr	Arg Ala	Ser Leu	Ara	Val Iv	2 G711	T T	03	II Tara	Tard	
	180									
				705		гур г	AR GI	еуп пув	Ly S	
Lys Lys Cys				185		гур г	лув G1 19	0	27.3	
	Val Val	Leu		185		пув т	ув GI 19	0 0	Dy 3	
	Val Val	Leu		185		r A P	ув GI 19	. о	2,3	
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gaa Glu	gtt Val 55	qac	ggt Gly	cgt Arg	cgc Arg	gta Val 60	gaa	ttg Leu	gcg Ala	ttg Leu	tgg Trp 65	gat Asp	act Thr	gct Ala	ggc Gly	308	3
caa Gln 70	qaa	gat Asp	tat Tyr	gat Asp	aga Arg 75	ttg	aga Arg	cca Pro	ctt Leu	tcg Ser 80	tac Tyr	cca Pro	gat Asp	tcc Ser	aac Asn 85	356	5
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gtg Val	atg Met	gaa Glu	aaa Lys 105	taa	atc Ile	tct Ser	gaa Glu	gtt Val 110	tta Leu	cac His	ttt Phe	tgt Cys	caa Gln 115	ggt Gly	gtt Val	452	2
cca Pro	atc Ile	atc Ile 120	ttg	gtt Val	ggt Gly	tgt Cys	aaa Lys 125	gca	gat Asp	ttg Leu	aga Arg	aat Asn 130	gat	cct Pro	caa Gln	500	)
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Gln	αca	caa Gln	gaa Glu	gtc Val	gct Ala 155	gac	caa Gln	atc Ile	ggt Gly	gct Ala 160	gtt	gac Asp	tac Tyr	atc Ile	gaa Glu 165	596	5
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	Tyr	Val 50	Ala	Asp	Val	Glu	Val 55	Asp	Gly	Arg	Arg	Val 60	Glu	Leu	Ala	Leu		
(	65			:		70	Glu				75					80		
					85		Val			90	•				95			,
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			115				Ile	120					125		-,			•
		130					Val 135					140		_				
=	145					150	Ala				155					160		
					165		Ser			170					175		:	
				180			Arg		185					190	_	_		
	:	цуз	195		1111	пуs	Ser	200	пуз	пур	пуз	тув	205	vaı	vai	Leu		
		0> 3: L> 1:												. •			•	,
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		L> CI 2> (:	)S L39).	(75	59)								÷					
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d	ggc	gct	jtc g	gcco	cegte	eg e	cetes	gegte	ctt	cct	cttc	ctct	tac	gcc a	agcto	agtga	3	120
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					CCC	Met 1	Ala	CCC	cqc		·							
A	lgg lrg	Gly	cga Arg	ccg					Cys	Gly 5		Ser	Lys	Gly	Arg 10	Gly		171
t	gc				atc Ile	cag Gln	cgc Arg	aag	Cys gtc Val	Gly 5 gtc	Ser gta	Ser	ggc Lys	Gly gac Asp	Arg 10 ggc	Gly		219
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. C		Gly	Lys 30	15 acg Thr	Ile agt Ser	Gln ctg Leu	Arg ctg Leu	aag Lys aac Asn 35	Cys gtc Val 20 gtc Val	Gly 5 gtc Val ttc Phe	Ser gta Val acg Thr	tgc Cys agg Arg	Lys ggc Gly ggg Gly 40	gac Asp 25 ttc Phe	Arg 10 ggc Gly ttc Phe	Gly gcg Ala acg Thr		219
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C G	ag 31n	Gly gtt Val 45 gac	Lys 30 tat Tyr	15 acg Thr gaa Glu cag	agt ser ccg Pro	Gln ctg Leu acg Thr	ctg Leu gtg Val 50 gag	aag Lys aac Asn 35 ttc Phe	Cys gtc Val 20 gtc Val gag Glu agt	Gly 5 gtc Val ttc Phe aac Asn ctc	ser gta Val acg Thr tac Tyr	tgc Cys agg Arg gtg Val 55 gat	Lys ggc Gly ggg Gly 40 cac His	Gly gac Asp 25 ttc Phe gat Asp	Arg 10 ggc Gly ttc Phe ctg Leu	gcg Ala acg Thr tat Tyr		219
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a I 6 g G	ag lln itc ile i0 gag	Gly gtt Val 45 gac Asp gag Glu atg	Lys 30 tat Tyr gac Asp ttc Phe ata	15 acg Thr gaa Glu cag Gln gac Asp tgc Cys	agt ser ccg Pro ctg Leu cgg Arg 80 ttc	Gln ctg Leu acg Thr gtg Val 65 cta Leu	Arg ctg Leu gtg Val 50 gag Glu cgg	aag Lys aac Asn 35 ttc Phe ctg Leu agc ser	Cys gtc Val 20 gtc Val gag Glu agt ctg Leu aat Asn	Gly 5 gtc Val ttc Phe aac Asn ctc Leu tcg ser 85 cca	ser gta Val acg Thr tac Tyr tgg Trp 70 tat Tyr acg	ser tgc Cys agg Arg gtg Val 55 gat Asp gca Ala	Lys ggc Gly ggg Gly 40 cac His acg Thr gaa Glu ctc	gac Asp 25 ttc Phe gat Asp gcg Ala acg Thr	Arg 10 ggc Gly ttc Phe ctg Leu ggg Gly cat His 90 aat	gcg Ala acg Thr tat Tyr cag Gln 75 gtg Val		<ul><li>219</li><li>267</li><li>315</li><li>363</li></ul>
o co co co co co co co co co co co co co	tc le io gag	Gly gtt Val 45 gac Asp Glu atg Met agc	Lys 30 tat Tyr gac Asp ttc Phe ata Ile aag	15 acg Thr gaa Glu cag Gln gac Asp tgc Cys 95 tgg	Ile agt Ser ccg Pro ctg Leu cgg Arg 80 ttc Phe ctc	Gln ctg Leu acg Thr gtg Val 65 cta Leu agc ser	Arg ctg Leu gtg Val 50 gag Glu cgg Arg gtc Val gag	aag Lys aac Asn 35 ttc Phe ctg Leu agc Ser gac Asp	Cys gtc Val 20 gtc Val gag Glu agt ctg Leu aat Asn 100 ttg	Gly 5 gtc Val ttc Phe aac Asn ctc Leu tcg Ser 85 cca Pro	ser gta Val acg Thr tac Tyr tgg Trp 70 tat Tyr acg Thr	ser tgc Cys agg Arg gtg Val 55 gat Asp gca Ala tcg ser tgt	Lys ggc Gly ggg Gly 40 cac His acg Thr gaa Glu ctc Leu ccg	Gly gac Asp 25 ttc Phe gat Asp gcg Ala acg Thr gag Glu 105 ggc	Arg 10 ggc Gly ttc Phe ctg Leu ggg Gly cat His 90 aat Asn	gcg Ala acg Thr tat Tyr cag Gln 75 gtg Val gtg		219 267 315 363 411
o c c a I 6 g G a I g G	tc le o gag lu tc le	Gly gtt Val 45 gac Asp gag Glu atg Met agc Ser	Lys 30 tat Tyr gac Asp ttc Phe ata Ile aag Lys 110	15 acg Thr gaa Glu cag Gln gac Asp tgc Cys 95 tgg Trp	agt Ser Ccg Pro ctg Leu cgg Arg 80 ttc Phe ctc Leu	ctg Leu acg Thr gtg Val 65 cta Leu agc ser gac Asp	ctg Leu gtg Val 50 gag Glu cgg Arg gtc Val gag Glu	aag Lys aac Asn 35 ttc Phe ctg Leu agc Ser gac Asp att Ile 115	Cys gtc Val 20 gtc Val gag Glu agt ctg Leu aat Asn 100 ttg Leu	Gly 5 gtc Val ttc Phe aac Asn ctc Leu tcg Ser 85 cca Pro gag Glu	ser gta Val acg Thr tac Tyr tgg Trp 70 tat Tyr acg Thr	tgc Cys agg Arg gtg Val 55 gat Asp gca Ala tcg ser tgt	Lys ggc Gly ggg Gly 40 cac His acg Thr gaa Glu ctc Leu ccg Pro 120	gac Asp 25 ttc Phe gat Asp gcg Ala acg Thr gag Glu 105 ggc Gly	Arg 10 ggc Gly ttc Phe ctg Leu ggg Gly cat His 90 aat Asn gtg Val	gcg Ala acg Thr tat Tyr cag Gln 75 gtg Val gtg Val		219 267 315 363 411 459
o c c c c c c c c c c c c c c c c c c c	tag ile io jag ilu itc ile ag ilu	Gly gtt Val 45 gac Asp gag Glu atg Met agc ser gta	Lys 30 tat Tyr gac Asp ttc Phe ata Ile aag Lys 110 ttg	15 acg Thr gaa Glu cag Gln gac Asp tgc Cys stgg Trp gtc	Ile agt Ser ccg Pro ctg Leu cgg Arg 80 ttc Phe ctc Leu gac	Gln ctg Leu acg Thr gtg Val 65 cta Leu agc ser gac Asp	Arg ctg Leu gtg Val 50 gag Glu cgg Arg gtc Val gag Glu	aag Lys aac Asn 35 ttc Phe ctg Leu agc gac Asp att Ile 115 tgt	Cys gtc Val 20 gtc Val gag Glu agt Ser ctg Leu aat Asn 100 ttg Leu gat	Gly 5 gtc Val ttc Phe aac Asn ctc Leu tcg ser 85 cca Pro gag Glu cta	Ser gta Val acg Thr tac Tyr tgg Trp 70 tat Tyr acg Thr	ser tgc Cys agg Arg gtg Val 55 gat Asp gca Ala tcg Ser tgt Cys	Lys ggc Gly ggg Gly 40 cac His acg Thr gaa Glu ctc Leu ccg pro 120 gac	Gly gac Asp 25 ttc Phe gat Asp GCG Asp GCG GCG GCG GCG GCG GCG GCG GCG GCG GC	Arg 10 ggc Gly ttc Phe ctg Leu ggg Gly cat His 90 aat Asn gtg Val gca	gcg Ala acg Thr tat Tyr cag Gln 75 gtg Val gtg Val aag Lys		219 267 315 363 411
C C C a I G C a I G C t L C	tc le so la company de la comp	Gly gtt Val 45 gac Asp gag Glu atg Met agcr gtal 125 gat	Lys 30 tat Tyr gac Asp ttc Phe ata Ile aag Lys 110 ttg Leu cgg	15 acg Thr gaa Glu cag Gln gac Asp tgc Cys 55 tgg Trp gtc Val cta	Ile agt Ser ccg Pro ctg Leu cgg Arg 80 ttc Phe ctc Leu gac Asp caa	Gln ctg Leu acg Thr gtg Val 65 cta Leu agc Ser gac Asp tca Ser cga	ctg Leu gtg Val 50 gag Glu cgg Arg gtc Val gag Glu aaa Lys	aag Lys aac Asn 35 ttc Phe ctg Leu agc Ser gac Asp att Ile 115 tgt	Cys gtc Val 20 gtc Val gag Glu agt Ser ctg Leu aat Asn 100 ttg Leu gat Asp	Gly 5 gtc Val ttc Phe aac Asn ctc Leu tcg Ser 85 cca Pro gag Glu cta Leu	ser gta Val acg Thr tac Tyr tgg Trp 70 tat Tyr acg Thr tac Tyr acg Arg	ser tgc Cys agg Arg gtg V55 gat Asp gca tcgr tgts cys exp 135 gat	Lys ggc Gly ggg Gly 40 cuis acg Thr gaa Glu ctc Leu crg Pro 120 gac Asp caa	gac Asp 25 ttc Phe gat Asp gcg Ala acg Thr gag Glu 105 ggc Gly cct Pro	Arg 10 ggc Cly ttc Phe ctg Leu ggg Cly cat His 90 aat Asn gtg Val gca Ala gaa	gcg Ala acg Thr tat Tyr cag Gln 75 gtg Val gtg Val aag Lys gta		219 267 315 363 411 459

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140 ggc Gly	ctc Leu	gly aaa	gtc Val	Ala	145 cga Arg	aga Arg	ata Ile	cga Arg	Ala	150 tca Ser	cga Arg	tac Tyr	tta Leu	gag Glu 170	155 tgc Cys		651
tcc Ser	tcc Ser	aaa Lys	cac His 175	160 aac Asn	cgg Arg	ggc Gly	gtt Val	aac Asn 180	165 gaa Glu	gtc Val	ttc Phe	tta Leu	cga Arg 185	ggc	cgc Arg		699
			act					agg						tcg Ser			747
tgt Cys			tago	cgcad	ect o	cacto	etegt	cc ag	gteta	agtco	2 220	aago	ccga	tega	acgctgc		806
gcts		ctc (	cccgt	tcgad	ec to	ctca	aactg	g cto	ctgc	ccca	ctat	gtca	aca (	ccaa	geggee		866
cato	gac	eeg 1	tccta	agac	ca ca	acta	cacag	g gt	gtta	ggac	gca	agaga	aac	tcca	gcg <b>c</b> gg		926
cccs	jacat	ccg	gtcc	ccat	gc to	cctg	ggcgt	t gta	agtg	cttc	gtg	cacto	ect (	gttc	gtaggt		986
gcgg	1999 <sup>†</sup>	tac	tcct	cccc	ac t	cgtg	cggt	g ct	caag	gacg	tgța	aggg	ggc :	agct	eggtge	,	1046
gcts	gtac	gaa	taag	ataga	at a	tata	cccc	c cc	accc	cgaa	ggt	cacai	tac	gcat	ggatat		1106
ctto	cacg	ctc :	aaat	atgt	ta c	gctc	cctt	a at	ctaa	ctgc	gtc	tata	atg	ggaa	ttgaat		1166
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<213> Schizophyllum commune

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 Met Ser Ser Cys Phe Gly Ser Lys Lys Pro Ile Tyr Arg Lys Ile
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gta att ctt ggt gat ggt gct gct ggt aaa acc agt ttg tta aat gta
                                                                          96
Val Ile Leu Gly Asp Gly Ala Ala Gly Lys Thr Ser Leu Leu Asn Val
                                  25
ttt act aag ggt tat ttc cct cag gta tac gag cct act ata ttt gaa
Phe Thr Lys Gly Tyr Phe Pro Gln Val Tyr Glu Pro Thr Ile Phe Glu
                              40
aac tac att cat gat atc ttt gtc gat gga aac agt ata gaa ctg tct
                                                                          192
Asn Tyr Ile His Asp Ile Phe Val Asp Gly Asn Ser Ile Glu Leu Ser
                         55
                                              60
cta tgg gat aca gct ggt caa gaa gag tat gat caa ctg cgt tcg tta
                                                                          240
Leu Trp Asp Thr Ala Gly Gln Glu Glu Tyr Asp Gln Leu Arg Ser Leu
                     70
                                          75
tca tat tca gat aca cat gtt att atg atc tgc ttt gcc gtg gat tca
                                                                         288
Ser Tyr Ser Asp Thr His Val Ile Met Ile Cys Phe Ala Val Asp Ser
                                      90
cga gac tca tta gaa aat gta atc aca aaa tgg ctt ccg gaa gtc tct
                                                                          336
Arg Asp Ser Leu Glu Asn Val Ile Thr Lys Trp Leu Pro Glu Val Ser
                                  105
agt aat tgc cct ggt gtt aaa ttg gtt ctt gtt gct cta aaa tgt gat
                                                                         384
Ser Asn Cys Pro Gly Val Lys Leu Val Leu Val Ala Leu Lys Cys Asp
                             120
                                                  125
tta cgt gga gct gat gag gag caa gtt gat cac agt aaa att att gat
Leu Arg Gly Ala Asp Glu Glu Gln Val Asp His Ser Lys Ile Ile Asp
                                                                         432
                         135
                                              140
tac gag gaa gga ctg gca gcg gca aaa aaa atc aac gct gta cga tat
                                                                         480
Tyr Glu Glu Gly Leu Ala Ala Lys Lys Ile Asn Ala Val Arg Tyr
145
                                          155
tta gaa tgc agc gct aaa tta aat cgt ggc gta aat gaa gct ttc acg
                                                                         528
Leu Glu Cys Ser Ala Lys Leu Asn Arg Gly Val Asn Glu Ala Phe Thr
                165
                                      170
gaa gct gca cgc gtt gcc ctt gcc gcg caa cca aga ggt aca aag gat
                                                                         576
Glu Ala Ala Arg Val Ala Leu Ala Ala Gln Pro Arg Gly Thr Lys Asp
            180
                                 185
ggt gct gat gaa tcc cat ggt acc gga tgt atc att gct tga
                                                                         618
Gly Ala Asp Glu Ser His Gly Thr Gly Cys Ile Ile Ala
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Val Ile Leu Gly Asp Gly Ala Ala Gly Lys Thr Ser Leu Leu Asn Val
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Ser Tyr Ser Asp Thr His Val Ile Met Ile Cys Phe Ala Val Asp Ser

90 85 Arg Asp Ser Leu Glu Asn Val Ile Thr Lys Trp Leu Pro Glu Val Ser 110 105 100 Ser Asn Cys Pro Gly Val Lys Leu Val Leu Val Ala Leu Lys Cys Asp 120 Leu Arg Gly Ala Asp Glu Glu Gln Val Asp His Ser Lys Ile Ile Asp 140. 135 130 Tyr Glu Glu Gly Leu Ala Ala Lys Lys. Ile Asn Ala Val Arg Tyr 155 160 150 Leu Glu Cys Ser Ala Lys Leu Asn Arg Gly Val Asn Glu Ala Phe Thr 170 165 Glu Ala Ala Arg Val Ala Leu Ala Ala Gln Pro Arg Gly Thr Lys Asp 180 185 Gly Ala Asp Glu Ser His Gly Thr Gly Cys Ile Ile Ala 200 205 <210> 341 <211> 582 <212> DNA <213> Emericella nidulans <220> <221> CDS <222> (1)..(582) <400> 341 atg gct gag atc cgc cgc aag ctt gtt atc gtt ggt gat ggt gcc tgc Met Ala Glu Ile Arg Arg Lys Leu Val Ile Val Gly Asp Gly Ala Cys 15 10 ggt aag acc tgt ctg ttg atc gtc ttc tca aag ggc act ttc cct gag 96 Gly Lys Thr Cys Leu Leu Ile Val Phe Ser Lys Gly Thr Phe Pro Glu 25 20 gtc tac gtc ccc acc gtc ttt gag aac tac gtt gcc gat gtt gag gtt 144 Val Tyr Val Pro Thr Val Phe Glu Asn Tyr Val Ala Asp Val Glu Val 45 40 gat ggc aag cac gtc gag ctc gct ctc tgg gat acg gct ggt caa gaa 192 Asp Gly Lys His Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu 60 gat tac gac cgt ctc cgc cct ctc tcc tac cct gac tcg cat gtc atc 240 Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Ser His Val Ile 75 70 ctg att tgc ttc gct gtc gac tca ccg gat tcc ctt gac aac gtt caa Leu Ile Cys Phe Ala Val Asp Ser Pro Asp Ser Leu Asp Asn Val Gln 288 90 85 gag aag tgg atc tct gaa gtc cta cac ttc tgc cag ggt ctc ccc atc 336 Glu Lys Trp Ile Ser Glu Val Leu His Phe Cys Gln Gly Leu Pro Ile 105 atc ctc gtc gga tgc aag aag gat ctt cgc cat gac ccc aag acg atc 384 Ile Leu Val Gly Cys Lys Lys Asp Leu Arg His Asp Pro Lys Thr Ile 120 432 gag gag ctg aac aag acc tct cag aag cct gtc acc ccc gaa cag ggt Glu Glu Leu Asn Lys Thr Ser Gln Lys Pro Val Thr Pro Glu Gln Gly 135 140 gag gaa gtc cgc aag aag att ggc gcc tac aag tac ctc gag tgc tct 480 Glu Glu Val Arg Lys Lys Ile Gly Ala Tyr Lys Tyr Leu Glu Cys Ser 155 150 145 get ega ace aac gag ggt gte egt gag gte ttt gag get gee aeg egt 528 Ala Arg Thr Asn Glu Gly Val Arg Glu Val Phe Glu Ala Ala Thr Arg 170 165 gct gcc ctc ttg acc aag acc cac aag agc aag aag aag tgc agc atc Ala Ala Leu Leu Thr Lys Thr His Lys Ser Lys Lys Cys Ser Ile 576 190 185 180 582 ctg taa

Leu

438

105

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Asp Gly Lys His Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu
Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Ser His Val Ile
Leu Ile Cys Phe Ala Val Asp Ser Pro Asp Ser Leu Asp Asn Val Gln
Glu Lys Trp Ile Ser Glu Val Leu His Phe Cys Gln Gly Leu Pro Ile
                                  105
                                                       110
Ile Leu Val Gly Cys Lys Lys Asp Leu Arg His Asp Pro Lys Thr Ile
                             120
Glu Glu Leu Asn Lys Thr Ser Gln Lys Pro Val Thr Pro Glu Gln Gly
                         135
                                              140
Glu Glu Val Arg Lys Lys Ile Gly Ala Tyr Lys Tyr Leu Glu Cys Ser
                     150
                                          155
Ala Arg Thr Asn Glu Gly Val Arg Glu Val Phe Glu Ala Ala Thr Arg
                 165
                                      170
Ala Ala Leu Leu Thr Lys Thr His Lys Ser Lys Lys Cys Ser Ile
Leu
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                                             Met Thr Ala Ala Gln
gee geg ggt gag gag geg eea eea gge gtg egg tee gte aag gtg gte
                                                                         102
Ala Ala Gly Glu Glu Ala Pro Pro Gly Val Arg Ser Val Lys Val Val
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ctg gtg ggc gac ggc tgc ggg aag acg tcg ctg ctg atg gtc ttc
Leu Val Gly Asp Gly Gly Cys Gly Lys Thr Ser Leu Leu Met Val Phe
                                                                         150
                                 .30
gee gat ggg gee tte eee gag age tae ace eee acg gtg ttt gag egg
                                                                         198
Ala Asp Gly Ala Phe Pro Glu Ser Tyr Thr Pro Thr Val Phe Glu Arg
tac atg gtc aac ctg caa gtg aaa ggc aaa cct gtg cac ctc cac atc
                                                                         246
Tyr Met Val Asn Leu Gln Val Lys Gly Lys Pro Val His Leu His Ile
tgg gac aca gca ggg caa gat gac tat gac cgc ctg cgg ccc ctg ttc
                                                                         294
Trp Asp Thr Ala Gly Gln Asp Asp Tyr Asp Arg Leu Arg Pro Leu Phe
70
                     75
                                          80
tac cct gac gcc agc gtc ctg ctt tgc ttc gat gtc acc agc ccg
                                                                         342
Tyr Pro Asp Ala Ser Val Leu Leu Leu Cys Phe Asp Val Thr Ser Pro
                                      95
aac age ttt gac aac atc ttt aac egg tgg tac eca gaa gtg aat cat
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Asn Ser Phe Asp Asn Ile Phe Asn Arg Trp Tyr Pro Glu Val Asn His
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110 ttc tgc aag aag gta ccc atc atc gtc gtg ggc tgc aag act gac ctg

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	cgc Arg	aag Lys 135	gac	aaa Lys	tca Ser	ctg Leu	gtg Val 140	aac	aag Lys	ctc Leu	cga Arg	aga Arg 145	aac	gga Gly	ttg Leu	gag Glu	48	86
	cct Pro 150	gtg	acc Thr	tac Tyr	cac His	agg Arg 155	ggc	cag Gln	gag Glu	atg Met	gcg Ala 160	agg Arg	tcc Ser	gtg Val	ggc Gly	gcg Ala 165	53	34
	gtg Val	gcc Ala	tac Tyr	ctc Leu	gag Glu 170	tgc Cys	tcg Ser	gct Ala	cgg Arg	ctc. Leu 175	cat His	gac Asp	aac Asn	gtc Val	cac His 180	gcc Ala	58	82
	gtc Val	ttc Phe	cag Gln	gag Glu 185	gcc Ala	gcc Ala	gag Glu	gtg Val	gcc Ala 190	ctc Leu	agc Ser	agc Ser	cgc Arg	ggt Gly 195	cgc Arg	aac Asn	63	30
	ttc Phe	tgg Trp	cgg Arg 200	Arg	att Ile	acc Thr	cag Gln	ggc Gly 205	ttt Phe	tgc Cys	gtg Val	gtg Val	acc Thr 210	tga	gegge	etc	6'	79
	ggg9	gcgto			acgc	gg ga	aaggg		g ggd	gct	gacc	tgc	tgct	gag (	ctgg	etggge	7:	39
	tgga	accc	ggt (	eccta	aggct	tg to	gacc	gccga	a act	tcca	etgc	aaca	agac	aaa (	egec	accaaa	79	99
	gcc	aggc	cet (	gagge	cctg	gg ag	gtcci	egga	c tga	agaa	aggg	ggt	tcct	ggg (	ccca	cctgct	8.	59
	ctg	tgta	aaa (	ctcg	teet	gc gg	gtgc	ccga	g aat	tcac	tcgc	taa	cccc.	tat (	gccc	ggtccc	9:	19
	gga	ccga	cat (	cctg	gagc	cg c	ctgt	gcag	c ct	gatg	cccc	ctc	gtgg	ctg	ctcc	cagggc	9	79
•	tgc:	acct	gcc :	agga	ccta	at g	ttct	tagg	t cc	ctct	ggcc	aga	accc	aca	cccg	gcccct ·	1	039
	tcc	cacc	tgt ·	cata	ctgg	ta a	ctgt	aaca	a ga	aaaa	cgac	atc	actt				1	086

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<212> PRT

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<213> Homo sapiens

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Met Thr Ala Ala Gln Ala Ala Gly Glu Glu Ala Pro Pro Gly Val Arg

Cys Lys Thr Asp Leu Arg Lys Asp Lys Ser Leu Val Asn Lys Leu Arg
130
135
140
130
130
140

Arg Asn Gly Leu Glu Pro Val Thr Tyr His Arg Gly Gln Glu Met Ala 145 150 155 160

Arg Ser Val Gly Ala Val Ala Tyr Leu Glu Cys Ser Ala Arg Leu His 165 170 175

Asp Asn Val His Ala Val Phe Gln Glu Ala Ala Glu Val Ala Leu Ser 180 185 Ser Arg Gly Arg Asn Phe Trp Arg Arg Ile Thr Gln Gly Phe Cys Val 200 Val Thr 210 <210> 345 <211> 1166 <212> DNA <213> Mus musculus <220> <221> CDS <222> (85)..(717) <400> 345 geogeoggge cagecegeg ecegeogeag ecagecegee gegtacegee tgetqeteeq 60 egeacegeeg teegeeagee aggg atg aac geg tee cag gtt geg gga gaa 111 Met Asn Ala Ser Gln Val Ala Gly Glu gag gcg ccg cag agc ggg cac tcg gtc aag gtg gtc ctg gtg ggc gac Glu Ala Pro Gln Ser Gly His Ser Val Lys Val Val Leu Val Gly Asp 159 10 15 20 ggg ggc tgc ggg aag acg tca ctg atg atg gtc ttc gcc aaa ggg gcc 207 Gly Gly Cys Gly Lys Thr Ser Leu Met Met Val Phe Ala Lys Gly Ala 30 35 ttc cca gag agc tac agt ccc aca gtg ttt gag cgc tat aat gcc act 255 Phe Pro Glu Ser Tyr Ser Pro Thr Val Phe Glu Arg Tyr Asn Ala Thr : 50 ctg cag atg aag ggt aaa cct gtg cac ctc caa atc tgg gac aca gcc 303 Leu Gln Met Lys Gly Lys Pro Val His Leu Gln Ile Trp Asp Thr Ala 65 70 ggg caa gat gac tat gac cgc ctc cgg ccc ttg ttc tat cct gat gcc 351 Gly Gln Asp Asp Tyr Asp Arg Leu Arg Pro Leu Phe Tyr Pro Asp Ala 80 85 aat gtc ttg ctc ctc tgc ttc gat gtg acc aat cca aac agc ttt gac 399 Asn Val Leu Leu Cys Phe Asp Val Thr Asn Pro Asn Ser Phe Asp 95 100 aac gtc tcc aac cgg tgg tac cca gag gtg aca cat ttc tgc aag gga Asn Val Ser Asn Arg Trp Tyr Pro Glu Val Thr His Phe Cys Lys Gly 447 110 115 gtg ccc atc att gtt gtg ggc tgc aag ata gac ctg cgt aag gac aag 495 Val Pro Ile Ile Val Val Gly Cys Lys Ile Asp Leu Arg Lys Asp Lys 125 130 135 gtg ctg gtg aac aac ctg cgg aag aaa aga ctg gag ccc gtg acc tac 543 Val Leu Val Asn Asn Leu Arg Lys Lys Arg Leu Glu Pro Val Thr Tyr 145 150 cac agg ggc cac gat atg gca agg tct gtg gga gcg gtg gcc tat ctt 591 His Arg Gly His Asp Met Ala Arg ServVal Gly Ala Val Ala Tyr Leu 160 gag tgt tca gct cgg ctc cat gac aac gtg gaa gca gtc ttc cag gaa 639 Glu Cys Ser Ala Arg Leu His Asp Asn Val Glu Ala Val Phe Gln Glu 175 180 gca gca gaa gtg gct ctc agc agt cgc aga cat aac ttt tgg cgg cgg 687 Ala Ala Glu Val Ala Leu Ser Ser Arg Arg His Asn Phe Trp Arg Arg 190 195 200 att act cag aat tgt tgc ttg gcc acc tgactggctt ggaacccacc 734 Ile Thr Gln Asn Cys Cys Leu Ala Thr 205 210 ttgccaaccg gtttactccg ctgcagaaag acccagaagc agaacttgta ctctgttgac 794

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tccaat	gagg	cctggcccct	ggaaccgaat	gaaacccggt	aatgatagga	aagaagtggt	914
cccaag	aacc	cttaagctct	ggaaaccaat	taatagaaca	tectgtgccc	aaatcctgaa	974
cctgcg	cctg	aacggggtct	gtgcggtctg	tttggcgcca	accttgtggc	taattctaat	1034
tgaagt	tata	tctacaggac	ctaagggttc	ccaagaacca	acttgcccgg	gctaataacc	1094
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<210> 346 <211> 210 <212> PRT

<213> Mus musculus

<400> 346 Met Asn Ala Ser Gln Val Ala Gly Glu Glu Ala Pro Gln Ser Gly His 15 Ser Val Lys Val Val Leu Val Gly Asp Gly Gly Cys Gly Lys Thr Ser 20 25 30 Leu Met Met Val Phe Ala Lys Gly Ala Phe Pro Glu Ser Tyr Ser Pro 40 45 Thr Val Phe Glu Arg Tyr Asn Ala Thr Leu Gln Met Lys Gly Lys Pro 55 Val His Leu Gln Ile Trp Asp Thr Ala Gly Gln Asp Asp Tyr Asp Arg 70 Leu Arg Pro Leu Phe Tyr Pro Asp Ala Asn Val Leu Leu Cys Phe 90 85 Asp Val Thr Asn Pro Asn Ser Phe Asp Asn Val Ser Asn Arg Trp Tyr 110 105 100 Pro Glu Val Thr His Phe Cys Lys Gly Val Pro Ile Ile Val Val Gly 120 125 Cys Lys Ile Asp Leu Arg Lys Asp Lys Val Leu Val Asn Asn Leu Arg ~140 130 135 Lys Lys Arg Leu Glu Pro Val Thr Tyr His Arg Gly His Asp Met Ala 155 150 Arg Ser Val Gly Ala Val Ala Tyr Leu Glu Cys Ser Ala Arg Leu His 175 165 170 Asp Asn Val Glu Ala Val Phe Gln Glu Ala Ala Glu Val Ala Leu Ser 185 190 180 Ser Arg Arg His Asn Phe Trp Arg Arg Ile Thr Gln Asn Cys Cys Leu 200

Ala Thr 210

<210> 347 <211> 735 <212> DNA

<213> Sus scrofa

<220> <221> CDS <222> (1)..(735)

atg aag gag aga aga gcc agc cag aaa tta tcc agt aaa tct atc atg
Met Lys Glu Arg Arg Ala Ser Gln Lys Leu Ser Ser Lys Ser Ile Met

1 5 10 15

Asp	Pro	Asn	Gln 20	Asn	Val	Lys	Cys	Lys 25	Ile	Val	Val	gtg Val	Gly 30	qaA	Ser		96
Gln	Суз	Gly 35	Arg	Thr	Ala	Leu	Leu 40	His	Val	Phe	Ala	45	Asp	Cys	Phe		144
Pro	Glu 50	Asn	Tyr	Val	Pro	Thr 55	Val	Phe	Glu	Asn	Tyr 60		Ala	Ser	Phe		192
gaa Glu 65	atc Ile	gac Asp	aca Thr	caa Gln	aga Arg 70	ata Ile	gaa Glu	ttg Leu	agc Ser	ctg Leu 75	tgg Trp	gac Asp	act Thr	tcg Ser	ggt Gly 80	•	240
tct Ser	cct Pro	tac Tyr	tat Tyr	gac Asp 85	aac Asn	gtc Val	cgg Arg	ccc Pro	ctc Leu 90	tcc Ser	tac Tyr	cca Pro	gac Asp	tca Ser 95	gac Asp		288
gcc Ala	gtg Val	ctg Leu	att Ile 100	Cya	Phe	gac Asp	atc Ile	agt Ser 105	aga Arg	cca Pro	gag Glu	act Thr	ctg Leu 110	gac Asp	agt Ser		336
Val	Leu	Lys 115	Lys	Trp	Lys	Gly	Glu 120	Ile	Gln	Glu	Phe	tgt Cys 125	Pro	Asn	Thr		384
aaa Lys	atg Met 130	ctc Leu	ttg Leu	gtc Val	ggc Gly	tgc Cys 135	aaa Lys	tct Ser	gat Asp	ctt Leu	cgg Arg 140	aca Thr	gat Asp	gtc Val	agt Ser		432
Thr 145	Leu	Val	Glu	Leu	Ser 150	Asn	His	Arg	Gln	Thr 155	Pro	gtt Val	Ser	Tyr	Asp 160		480
Gln	Gly	Ala	Asn	Met 165	Ala	Lys	Gln	Ile	Gly 170	Ala	Ala	act Thr	Tyr	Ile 175	Glu		528
Cys	Ser	Ala.	Leu 180	Gln	Ser	Glu	Asn	Ser 185	Val	Arg	Asp	att Ile	Phe 190	His	Val	· .	576
gcc Ala	acc Thr	ttg Leu 195	gca Ala	tgt Cys	gta Val	aat Asn	aag Lys 200	aca Thr	aat Asn	aaa Lys	aac Asn	gtt Val 205	aag Lys	cgg Arg	aac Asn		624
												ccc Pro					672
gaa Glu 225	ctc Leù	tcg Ser	gca Ala	gtg Val	gct Ala 230	acg Thr	gac Asp	tta Leu	cga Arg	aag Lys 235	gac Asp	aaa Lys	gcc Ala	aag Lys	agc Ser 240		720
_	act Thr		_	tga	٠		•	٠.									735

<210> 348

<211> 244

<212> PRT

<213> Sus scrofa

<400> 348

Met Lys Glu Arg Arg Ala Ser Gln Lys Leu Ser Ser Lys Ser Ile Met 10 Asp Pro Asn Gln Asn Val Lys Cys Lys Ile Val Val Val Gly Asp Ser 20 25 Gln Cys Gly Arg Thr Ala Leu Leu His Val Phe Ala Lys Asp Cys Phe 40 Pro Glu Asn Tyr Val Pro Thr Val Phe Glu Asn Tyr Thr Ala Ser Phe 55 Glu Ile Asp Thr Gln Arg Ile Glu Leu Ser Leu Trp Asp Thr Ser Gly Ser Pro Tyr Tyr Asp Asn Val Arg Pro Leu Ser Tyr Pro Asp Ser Asp 85 90 Ala Val Leu Ile Cys Phe Asp Ile Ser Arg Pro Glu Thr Leu Asp Ser 105 Val Leu Lys Lys Trp Lys Gly Glu Ile Gln Glu Phe Cys Pro Asn Thr

								2	58/29	1								
	Lys :	Met-	115	T.011	va1	Glv	Cvs	120 Lvs	Ser	Asp	Leu	Ara	125 Thr	Asp	Val	Ser		
	-	130					135		Arg			140						
	145					150					155					160		
		_			165				Ile	170					175			
	Cys	Ser	Ala	Leu 180	Gln	Ser	Glu	Asn	Ser 185	Val	Arg	Asp	Ile	Phe 190	His	Val		
			195		_			200	Thr				205					
	_	Ser 210	Gln	Arg	Ala	Thr	Lys 215	Arg	Ile	Ser	His	Met 220	Pro	Ser	Arg	Pro		
	Glu 225	Leu	Ser	Ala	Val	Ala 230	Thr	qeA	Leu	Arg	Lys 235	Asp	Lys	Ala	Lys	Ser 240		
	Cys	Thr	Val	Met								_						
•				•••		•			,									
	<210 <211 <212 <213	> 10 > DI	)17 NA	sapie	ens			•										
	<220 <221 <222	.> CI		. (665	5)													
	<400	)> 34	19															
	gccg	ccg	cca	gtgct	geg	gg c	teeg	ggca		gat Asp	gcc Ala	ccc Pro	gjà aaa	gcc Ala	ctg Leu	gcc Ala		53
	саσ	acc	acc	gcc	ccc	aat	cca	aac	1 agg	aaq	gag	ctg	aag	atc	gtg	atc		101
	Gln	Thr	Ala	Ala	Pro	Gly	Pro 15	Gly	Arg	Lys	Glu	Leu 20	Lys	Ile	Val	Ile		
	gtg Val	aac	gac Asp	ggc Gly	ggc Gly	tgc Cys	ggc Gly	aag Lys	acc Thr	tcg Ser	ctg Leu	ctc Leu	atg Met	gtg Val	tac Tyr	ser		149
	25					30			gcc		35					40		197
	Gln	Gly	Ser	Phe	Pro	Glu	His	Tyr	Ala	Pro	Ser	Val	Phe	Glu	Lys 55	Tyr		
	acg Thr	gcc Ala	agc Ser	gtg Val	acc	gtt Val	ggc Gly	agc Ser	aag Lys	gag Glu	gtg Val	acc Thr	ctg Leu	aac Asn	ctc Leu	tac Tyr		245
				60					65 gac					70				293
	gac Asp	acg Thr	gcc Ala 75	GJÀ	Gln	Glu	Asp	Tyr 80	Asp	Arg	Leu	Arg	Pro 85	Leu	Ser	Tyr		233
	cag	aac	acc	cac His	ctc	gtg	ctc Leu	ato	tgc Cys	tat Tyr	gac Asp	gtc Val	atg	aat Asn	ccc	acc		341
		90					95					100		•				389
	Ser	tac Tyr	gac Asp	aac Asn	yal Val	Leu	Ile	aag Lys	tgg Trp	Phe	Pro	Glu	Val	Thr	His	Phe 120		369
	105 tqc	cac	ggg	atc	ccc	110 atg	gtg	cto	atc	ggc	tgc	aag	aca	gac	ctg	agg		437
	Cys	Arg	Gly	Ile	Pro 125	Met	. Val	. Leu	lle	Gly 130	Cys	Lys	Thr	Asp	135	arg		
	Lys	Asp	Lys	Glu 140	Glr	Leu	Arg	l Pàs	Leu 145	Arg	Ala	Ala	Glr	150	GIU	r ccc		485
	atc Ile	acc Thr	tac Tyr 155	atg Met	cac	ggc ggc	cto Lev	ago Ser 160	: Ala	tgc Cys	gaa Glu	Glr	ato Ile 165	Arg	gct Ala	gct Ala		533
	ctc Leu	tac	cto	gaa	tgt Cys	tco Ser	: Ala	aag Lys	r ttt	cgg Arg	gag Glu	l Asr	gtg Val	gag	gac Asp	gtc Val		581
	ttc	170 cgg	gaq	gee	gco	aag	175 gtg	get	cto	ago	gct	180	, aac	aag	gcg	caa		629
	Phe 185		Glu	ı Ala	Ala	190 190		Ala	. Leu	. ser	Ala 195	. шет ;	тъх	• гАг	, ATS	Gln 200		
	cgg	cag	aag	r aag	cgo			tgo	ctg	cto			accca	ggg	caga	acagac	2	682

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PCT/EP2004/008136
                                259/291.
Arg Gln Lys Lys Arg Arg Leu Cys Leu Leu Leu
tcacgacage actgacaggg cccgggggcc caggtgccga ttgcaccagg gaggctgccc
                                                                        742
catecegace etecagetea tggtgtetgg ggeetgegge tagactettg gaacattetg
                                                                        802
gaactetete ettteetgge tggggetetg accacaaact eccetecagg etgeceetgg
                                                                        862
gacatggtgg tgatgtgggt gcaggagcca gtgtctgttg tcgggactcg caagtgccct
                                                                        922
catcacagec acceccacca egagtgtete eccagtgeag acteaagtta tgettgaaat
                                                                        982
gaaaaagtict atctggtagt gggtaaaaaa aaaaa
                                                                        1017
<210> 350
<211> 211
<212> PRT
<213> Homo sapiens
<400> 350
Met Asp Ala Pro Gly Ala Leu Ala Gln Thr Ala Ala Pro Gly Pro Gly
Arg Lys Glu Leu Lys Ile Val Ile Val Gly Asp Gly Gly Cys Gly Lys
Thr Ser Leu Leu Met Val Tyr Ser Gln Gly Ser Phe Pro Glu His Tyr
                            40
Ala Pro Ser Val Phe Glu Lys Tyr Thr Ala Ser Val Thr Val Gly Ser
Lys Glu Val Thr Leu Asn Leu Tyr Asp Thr Ala Gly Gln Glu Asp Tyr
                                         75
Asp Arg Leu Arg Pro Leu Ser Tyr Gln Asn Thr His Leu Val Leu Ile
                85
                                    90
Cys Tyr Asp Val Met Asn Pro Thr Ser Tyr Asp Asn Val Leu Ile Lys
            100
                                105
                                                     110
Trp Phe Pro Glu Val Thr His Phe Cys Arg Gly Ile Pro Met Val Leu
                            120
Ile Gly Cys Lys Thr Asp Leu Arg Lys Asp Lys Glu Gln Leu Arg Lys
                        135
                                             140
Leu Arg Ala Ala Gln Leu Glu Pro Ile Thr Tyr Met Gln Gly Leu Ser
                    150
                                         155
Ala Cys Glu Gln Ile Arg Ala Ala Leu Tyr Leu Glu Cys Ser Ala Lys
                165
                                    170
Phe Arg Glu Asn Val Glu Asp Val Phe Arg Glu Ala Ala Lys Val Ala
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185 Leu Ser Ala Leu Lys Lys Ala Gln Arg Gln Lys Lys Arg Arg Leu Cys 195

Leu Leu Leu 210 <210> 351 <211> 684

<212> DNA

<213> Mus musculus

<220> <221> CDS <222> (1)..(684)

<400> 351 atg gag ggg cag agt ggc cgc tgc aag atc gta gtg gtg ggg gac gcg

							2	260/29	<b>)1</b>							
Met 1	Glu	Gly	Gln	Ser 5	Gly	Arg	Cys	Lys	Ile 10	Val	Val	Val	Gly	Asp 15	Ala	
gag Glu	Cys	Gly	Lys 20	Thr	Ala	Leu	Leu	Gln 25	Val	Phe	Ala	aag Lys	Asp 30	Ala	lyr	96
Pro	Gly	Ser	Tyr	Val	Pro	Thr	Val	Phe	Glu	Asn	Tyr	act Thr 45	Ala	ser	Pne	144
Glu	Ile 50	qeA	Lys	Arg	Arg	Ile 55	Glu	Leu	Asn	Met	Trp 60	gat Asp	Thr	Ser	GIÄ	. 192
Ser 65	Ser	Tyr	Tyr	Asp	Asn 70	Val	Arg	Pro	Leu	Ala 75	Tyr	ccg Pro	Asp	Ser	Asp 80	240
Āla	Val	Leu	Ile	Cys 85	Phe	Asp	Ile	Ser	Arg 90	Pro	Glu	aca Thr	Leu	Asp 95	Ser	288
Val	Leu	Lys	Lys 100	Trp	Gln	Gly	Glu	Thr 105	Gln	Glu	Phe	tgc Cys	Pro 110	Asn	Ala	336
Lys	Val	Val 115	Leu	Val	Gly	Cys	Lys 120	Leu	Asp	Met	Arg	act Thr 125	Asp	Leu	Ala	384
Thr	Leu 130	Arg	Glu	Leu	Ser	Lys 135	Gln	Arg	Leu	Ile	Pro 140	Val	Thr	His		432
Gln 145	Gly	Thr	Val	Leu	Ala 150	Lys	Gln	Val	Gly	Ala 155	Val	tcc Ser	Tyr	Val	Glu 160	480
Cys	Ser	Ser	Arg	Ser : 165	Ser	Glu	Arg	Ser	Val 170	Arg	Asp	gtc Val	Phe	His 175	Val	528
Ala	Thr	Val	Ala 180	Ser	Leu	Gly	Arg	Gly 185	His	Arg	Gln	cta Leu	Arg 190	Arg	Thr	576
Asp	Ser	Arg	Arg	Gly	Leu	Gln	Arg 200	Ser	Thr	Gln	Leu	tcg Ser 205	Gly	Arg	Pro	624
gac Asp	cgg Arg 210	gga Gly	aat Asn	gag Glu	ggc	gag Glu 215	Met	cat His	aag Lys	gat Asp	cga Arg 220	gcc Ala	aag Lys	agc Ser	tgt Cys	672
	ctc Leu															684

<210> 352

<211> 227

<212> PRT

<213> Mus musculus

<400> 352 Met Glu Gly Gln Ser Gly Arg Cys Lys Ile Val Val Val Gly Asp Ala 10 Glu Cys Gly Lys Thr Ala Leu Leu Gln Val Phe Ala Lys Asp Ala Tyr 30 25 20 Pro Gly Ser Tyr Val Pro Thr Val Phe Glu Asn Tyr Thr Ala Ser Phe 45 40 Glu Ile Asp Lys Arg Arg Ile Glu Leu Asn Met Trp Asp Thr Ser Gly 60 55 Ser Ser Tyr Tyr Asp Asn Val Arg Pro Leu Ala Tyr Pro Asp Ser Asp 75 65 Ala Val Leu Ile Cys Phe Asp Ile Ser Arg Pro Glu Thr Leu Asp Ser 90 85 Val Leu Lys Lys Trp Gln Gly Glu Thr Gln Glu Phe Cys Pro Asn Ala 110 100 105 Lys Val Val Leu Val Gly Cys Lys Leu Asp Met Arg Thr Asp Leu Ala 115

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Thr Leu Arg Glu Leu Ser Lys Gln Arg Leu Ile Pro Val Thr His Glu
                          135
Gln Gly Thr Val Leu Ala Lys Gln Val Gly Ala Val Ser Tyr Val Glu
                     150
                                           155
Cys Ser Ser Arg Ser Ser Glu Arg Ser Val Arg Asp Val Phe His Val
                                       170
Ala Thr Val Ala Ser Leu Gly Arg Gly His Arg Gln Leu Arg Arg Thr
                                   185
Asp Ser Arg Arg Gly Leu Gln Arg Ser Thr Gln Leu Ser Gly Arg Pro
                              200
                                                    205
Asp Arg Gly Asn Glu Gly Glu Met His Lys Asp Arg Ala Lys Ser Cys
    210
                          215
                                               220
Asn Leu Met
225
<210> 353
<211> 576
<212> DNA
<213> Brachydanio rerio
<220>
<221> CDS
<222> (1)..(576)
<400> 353
atg cag acg att aag tgt gtg gtg gga gac ggt gca gta ggc aag
                                                                           · 48
Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys
                                      10
aca tgc ctt ctt att tct tat acg aca aat gcc ttt cca gag gag tac
                                                                           96
Thr Cys Leu Leu 11e Ser Tyr Thr Thr Asn Ala Phe Pro Glu Glu Tyr
                                   25
att ccc aca gtg ttt gac aac tac agt gct cag atg agt gta gat ggg
                                                                           144
Ile Pro Thr Val Phe Asp Asn Tyr Ser Ala Gln Met Ser Val Asp Gly
                              40
cgc act gtc agc ctc aac ctc tgg gac acg gca ggg cag gag gag tat
Arg Thr Val Ser Leu Asn Leu Trp Asp Thr Ala Gly Gln Glu Glu Tyr
                                                                          · 192
                         55
                                               60
gac cgt ctg cgc acg ctt tcc tac cca caa act aat gtt ttc atc att
                                                                           240
Asp Arg Leu Arg Thr Leu Ser Tyr Pro Gln Thr Asn Val Phe Ile Ile
                                           75
tgc ttt tcc atc gga agc cct tca tca tta gct aat gtt cgc cac aag
                                                                           288
Cys Phe Ser Ile Gly Ser Pro Ser Ser Leu Ala Asn Val Arg His Lys
                 85
                                       90
tgg cac ccg gag gtg tct cac cac tgt ccc aac gtg cca att ctt cta
                                                                           336
Trp His Pro Glu Val Ser His His Cys Pro Asn Val Pro Ile Leu Leu
            100
                                  105
                                                        110
gtt ggc acc aag aag gat ctg cgt tca gat aca gag aca att aag aag
                                                                           384
Val Gly Thr Lys Lys Asp Leu Arg Ser Asp Thr Glu Thr Ile Lys Lys
        115
                              120
                                                   125
ttg aag gag caa ggg ctt gca ccc tct act caa cag cag ggt ggc acc
                                                                           432
Leu Lys Glu Gln Gly Leu Ala Pro Ser Thr Gln Gln Gln Gly Thr
    130
                         135
                                               140
ctg tgc aag cag atc aat gct gtg agg tat ctg gag tgc tcg gcg ctc
                                                                           480
Leu Cys Lys Gln Ile Asn Ala Val Arg Tyr Leu Glu Cys Ser Ala Leu
                     150
                                           155
ege cag gaa gge gtg egg gat gtg ttt gta gat get gtt egt get gtg
                                                                           528
Arg Gln Glu Gly Val Arg Asp Val Phe Val Asp Ala Val Arg Ala Val
                 165
                                      170
ctc tac ccc atg acc aaa aag aat acc aag aag tgt gtt ctc tta
Leu Tyr Pro Met Thr Lys Lys Asn Thr Lys Lys Cys Val Leu Leu
                                                                           573
                                  185
tag
                                                                           576
```

<210> 354 <211> 191 <212> PRT <213> Brachydanio rerio

Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys · 10 Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Ala Phe Pro Glu Glu Tyr 25 20 Ile Pro Thr Val Phe Asp Asn Tyr Ser Ala Gln Met Ser Val Asp Gly 40 Arg Thr Val Ser Leu Asn Leu Trp Asp Thr Ala Gly Gln Glu Glu Tyr 55 60 Asp Arg Leu Arg Thr Leu Ser Tyr Pro Gln Thr Asn Val Phe Ile Ile 70 Cys Phe Ser Ile Gly Ser Pro Ser Ser Leu Ala Asn Val Arg His Lys 90 85 Trp His Pro Glu Val Ser His His Cys Pro Asn Val Pro Ile Leu Leu 105 Val Gly Thr Lys Lys Asp Leu Arg Ser Asp Thr Glu Thr Ile Lys Lys 125 120 115 Leu Lys Glu Gln Gly Leu Ala Pro Ser Thr Gln Gln Gln Gly Gly Thr 140 135 130 Leu Cys Lys Gln Ile Asn Ala Val Arg Tyr Leu Glu Cys Ser Ala Leu 155 150 Arg Gln Glu Gly Val Arg Asp Val Phe Val Asp Ala Val Arg Ala Val 170 165 Leu Tyr Pro Met Thr Lys Lys Asn Thr Lys Lys Cys Val Leu Leu 185 180

<213> Xenopus laevis

<220>
<221> CDS
<222> (1)..(576)

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145					150					155					160		
Asn	Gln	Asp	Cly	Ile 165	Lys	Glu	Val	Phe	Ala 170	Asp	Ala	Val	Arg	gct Ala 175			528
ctc Leu	aac Asn	ccg Pro	act Thr 180	ccc Pro	atc Ile	aag Lys	gac Asp	aaa Lys 185	aag Lys	agc Ser	tgc Cys	ttc Phe	att Ile 190	ttg Leu			573
tga												1					576
						•			•		•					-	•.
	ė									·. · .							
<21:	0 > 3: 1 > 1: 2 > P!	91 RT		- ovrd					Œ	·						· · · · · · · · · · · · · · · · · · ·	
		enop			-											-	
	0 > 3!		T10		<b>~</b>	77-7	17- 1	**- 1	<b>63</b>	3	~1		**- 7	<b>63</b>	•		
Met 1	GIII	ser	TTE	БуS	Cys	vaı	vai	var	10	Asp	GTA	Ala	vaı	Gly 15	гÀг		
Thr	Сув	Leu	Leu 20	Ile	Cys	Phe	Thr	Thr 25	Asn	Ala	Phe	Pro	Lys	Glu	Tyr	•	
Ile	Pro	Thr		Phe	Asp	Asn	Tyr		Ala	Gln	Thr	Ala 45	Val	Asp	Gly	-	
Arg	Thr 50		Ser	Leu	Asn	Leu 55	Trp	Asp	Thr	Ala	Gly	-	Glu	Glu	Tyr		
Asp 65		Leu	Arg	Thr	Leu 70		Tyr	Pro	Gln		Asn	Val	Phe	Ile		. *	
	Phe	Ser	Ile			Pro	Thr	Ser	_	75 Glu	Asn	Val	Lys	His	Lys 80		
Trp	Tyr	Pro		85 Val	Gly	His	His		90 Pro	Asn	Val	Pro		95 Leu	Leu	•	
Val	Gly		100 Lys	Lys	Asp	Leu	Arg	105 Asn	Asn	Ala	Asp		110 Ile	Lys	Lys		
Len	Lvs	115 Glu	Gln	Asn	Gln	Met	120 Pro	Tle	Thr	Δεη	Hig	125 Gln	Glv	Gly	λan	•	
-	130					135					140			Ala			
145	AIa	шуs	GIII	TTE	150	MIG.	val	пуs	TÄT	155	GIU	Cys	ser	MIG.	160		
Asn	Gln	Asp	Gly	Ile 165	Lys	Glu	Val	Phe.	Ala 170	Asp	Ala	Val	Arg	Ala 175	Val		
Leu	Asn	Pro	Thr 180	Pro	Ile	Lys	Asp	Lys 185	Lys	Ser	Cys	Phe	Ile 190	Leu			
	)> 35																
	L> 59 2> DN																
		nopu	ıs tı	ropic	alis	3											
<220	)>																
<221	-> 'CI														٠		
<222	?> (1	L) (	(591)	)													
<400	)> 35	57															
									Val					gct Ala			48
	aaa	acc	tgc	ctc	ctc	atc	gtc	ttc	10 agc	aag	gac	gag	ttc	15 ccc	qag		96
														Pro			
														gag Glu			144
		35					40					45					100
Asp	Val 50	Lys	Gln	Val	Glu	Leu	Ala	Leu	Trp	Asp	Thr	Ala	GJÀ	cag Gln	gag Glu		192
	tac													gtc			240
Asp 65	Tyr	Asp	Arg	Leu	Arg 70	Pro	Leu	Ser	Tyr	Pro 75	Asp	Thr	Asp	Val	Ile 80		

							-		_								
	atg Met																288
	aag Lys																336
	ctg Leu																384
	gag Glu 130															•	432
	gcc Ala																480
gcc Ala	aag Lys	acc Thr	aag Lys	gaa Glu 165	ggg	gtc Val	cgg Arg	gag Glu	gtg Val 170	ttc Phe	gaa Glu	acg Thr	gcc Ala	act Thr 175	agg Arg		528
	gcg Ala																576
_	aag Lys		ctc	tga													591

<210> 358 <211> 196 <212> PRT

<213> Xenopus tropicalis

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<210> 359 <211> 735 <212> DNA <213> Xenopus laevis

195

<220>
<221> CDS
<222> (1)..(735)

<400	)> 3	59															
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Met 1	Lys	Glu	Arg	Arg 5	Thr	Ser	Gln	Lys	Leu 10	Āla	Ser	ГÀЗ	Ser	Met 15	Met		
gat	ccc	aac	cag	aat	gtg	aaa	tgt	aaa		qtq	qtq	qtq	qqq		agc .		96
Asp	Pro	Asn	Gln 20	Asn	Val	Lys	Cys	Lys 25	Ile	Val	Val	Val	Gly	Asp	Ser		
cag	tgt	ggc	aaa	act	gcc	ctg	ctc	cat	gtc	ttt	gcc	aag	gac	tcc	ttc		144
	Cys	35	_				40	•				45	_				÷
ccà	gag	aac	tat	gtc	CCC	acc	gta	ttt	gag	aat	tac	acg	gcc	agt	ttt	-	192
	Glu 50		-			55					60						
gaa	att	gac	acg	cag	agg	ata	gaa	ctg	agt	ctc	tgg	gat	aca	tct	ggt		240
65	Ile				70					75	_	_			80		
	cct																288.
Ser	Pro	Tyr	Tyr	Asp 85	Asn	Val	Arg	Pro	Leu 90	Ser	Tyr	Pro	Asp	Ser 95	Asp		
_	gtt	_		_		_		_	_					_			336
:	Val		100	_		_		105					1,10	-	•		
	ctt																384
Val	Leu	Lys 115	Lys	Trp	Lys	Gly	Glu 120	Ile	Gln	Glu	Phe	Cys 125	Pro	Asn	Thr		
	atg	_	_	_		_			_		_		_				432
_	Met 130				_	135	_		_		140						
	tta																480
145	Leu	vaı	GIU	Leu	150		HIS	Arg	GILL	155	Pro	vaı	ser	ıyr	_		
	ggg.	aca	aac	ato			cad	ata	aga		acc	aca	tac	atc	160		528
	Gly																220
	•			165		1			170		•		-	175			
_	tct			_				_	_	_	_				_		576
Cys	Ser	Ala	Leu 180	Gln	Ser	Glu	Asn	Ser 185	Val	Arg	Asp	Ile	Phe 190	His	Val		
	acc																624
Ala	Thr	Leu 195	Ala	Cys	Val	Asn	<b>Lys</b> 200	Thr	Asn	Lys	Asn	Leu 205	Lys	Arg	Asn		
	act																672
Lys	Thr 210	Gln	Arg	Ala	Thr	Lys 215	Arg	Ile	Ser	His	Met 220	Pro	Ser	Arg	Pro		
	cta																720
	Leu	Ser	Ala	Val		Thr	Asp	Leu			Asp	Lys	Ala	Lys			
225				<b>.</b>	230					235					240		<b>~</b> ~ ~
_	agc Ser	_	_	rga											•		735
~y∋	∴-T	TTC	1-10-0									•					

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<210> 360
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<400> 360

<sup>&</sup>lt;211> 244

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Xenopus laevis

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 Arg
 Arg
 Thr
 Ser
 Gln
 Lys
 Leu
 Ala
 Ser
 Lys
 Ser
 Met
 Met

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 10
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								2	66/29	1								•
					85					90					95			
	Ala	Val	Leu	Ile 100		Phe	Asp		Ser 105	Arg	Pro	Glu	Thr	Leu 110	qaA	Ser		
	Val	Leu	Lys 115	Lys	Trp	Lys		Glu 120	Ile	Gln	Glu	Phe	Cys 125	Pro	Asn	Thr		
	Lys	Met 130	Leu	Leu	Val	Gly	Cys 135	Lys	Ser	Asp	Leu	Arg 140	Thr	Asp	Leu	Thr		
	Thr 145	Leu	Val	Glu	Leu	Ser 150	Asn	His	Arg	Gln	Thr 155	Pro	Val	Ser	Tyr	Asp 160		
	Gln	Gly	Ala	Asn	Met 165		Lys	Gln	Ile	Gly 170	Ala	Ala	Thr	Tyr	Ile 175	Glu		
	Cys	Ser	Ala	Leu 180		Ser	Glu	Asn	Ser. 185	Val	Arg	Asp	Ile	Phe 190	His	Val		
			195	Ala				200		Asn			205					
	_	210					215			Ser		220						
• -	Glu 225	Leu	Ser	Äla	Val	Ala 230	Thr	Asp	Leu	Arg	Lys 235	qaA	ГÀЗ	Ala	ГÀЗ	Ser 240		
	Cys	Ser	Ile	Met											•		•	
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		L> 10 2> DI															•	
	<213	3> Pa	agru	s ma	jor	•											•	
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	<222	2> (:	25).	. (60	3)													
	<40	0> 3 cacg	61 agg	cgca	gegġ	aa ca	1	atg o Met (	cag	gct a Ala :	atc a	aaa Lys	tgt ( Cys )	gtg g Val	gtc y Val	gtg Val		51
	Gly	gat Asp	gga Gly	gct Ala	gtg Val	gga Gly 15	aaa	aca	tgt Cys	ctt Leu	ctc Leu 20	atc Ile	agc Ser	tac Tyr	aca Thr	acc Thr 25		99
	10 aat Asn	gcc Ala	ttc Phe	ccc Pro	Gly	gag	tac Tyr	att Ile	cct Pro	act Thr 35	gta	ttt Phe	gac Asp	aac Asn	tac Tyr 40	tca		147
	gct Ala	aat Asn	gtg Val	atg Met	30 gtg Val	gac Asp	agc Ser	aag Lys	cca Pro	gtc Val	aac Asn	ctg Leu	ggc Gly	Leu	tgg	gat Asp		195
	aca	gct	gga	45 cag	gaa	gac	tac	gac	50 agg	ctc	cgc	cca	ctg	55 tcc	tac	cca		243
			60					65		Leu			70					291
	Gln	Thr	Asp	Val	Phe	Leu	Ile 80	Cys	Phe	tcc Ser	Leu	Val 85	Ser	Pro	Ala	Ser		291
	Tyr	gag	aac Asn	gto Val	aga Arg	Ala	aag Lys	tgg Trp	tac Tyr	cca Pro	gag Glu 100	Val	cgc Arg	cac His	cac His	tgc Cys 105		339
	90	tcc	aca	cct	ato	95 atc	ctg	gtg	ggc	acc	aag	ctg	gat	ctg	agg	gac		387
					110	)				Thr 115					120	)		435
	gag Glu	Lys	gaa Glu	acc Thr	Ile	gag Glu	Lys	Leu	Lys 130	Glu	Lys	Lys	Leu	135	Pro	atc Ile		100
	acc Thr	tac Tyr	c ccc	cac	aac	ctg Leu	gct Ala	Leu	Ala	aag Lys	gag Glu	ato l Ile	: Asp	Ala	gtg Val	aag Lys		483
	tac	cts	140 g gag	ta	tca	gcc	tto	145 acc	cac	g cgt	ggc	cto	150 aag	aco	gto	ttc Phe		531
	_	155	5				160	)				165	5			aag		579
	gac Asp 170	Gli	ı Ala	a Ile	Arg	g gcc g Ala 175	ı Val	L Lev	. Cys	Pro	180	Pro	Thr	Lys	val	Lys 185		

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cgatgagaaa gcgtttgcga ctgatgaaaa ggtgaaaaga agacgatggg aaagttctgt	690
tatgtttaat ggtttgtgat agaagactgc gactagattt ccactaggtt agaaaaaat	750
aatgcttgtg cggtgatgat aaatggtaaa tggtagcaaa ccctttctgt acagcatact	810
ctgagactga ttattcaagt gcattataga ccaggcagac atttcactgt aaaattgaac	870
aaagtatatc actagatgtg gaggctgaca cactgtacat tcatcctgtg ggcttaaatg	930
gtcagatcaa gagcagcaaa gcacctgcac aacggactct gctgtccctt ttggggctga	990
cagtatgtac acaggtgtct tgtgcggctt cacataatga taata	1035

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<210> 362
<211> 192
<212> PRT
<213> Pagrus major
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<400> 362

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 Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Ala Phe Pro Gly Glu Tyr

 20
 25
 30

 Ile Pro Thr Val Phe Asp Asn Tyr Ser Ala Asn Val Met Val Asp Ser

 35
 45

 Lys Pro Val Asn Leu Gly Leu Trp Asp Thr Ala Gly Gln Glu Asp Tyr

 50

Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Ile 65 70 75 80

Cys Phe Ser Leu Val Ser Pro Ala Ser Tyr Glu Asn Val Arg Ala Lys 85 90 95

Trp Tyr Pro Glu Val Arg His His Cys Pro Ser Thr Pro Ile Ile Leu

Val Gly Thr Lys Leu Asp Leu Arg Asp Glu Lys Glu Thr Ile Glu Lys

115 120 125
Leu Lys Glu Lys Lys Leu Ala Pro Ile Thr Tyr Pro Gln Gly Leu Ala

Leu Ala Lys Glu Ile Asp Ala Val Lys Tyr Leu Glu Cys Ser Ala Leu

145 150 155 160
Thr Gln Arg Gly Leu Lys Thr Val Phe Asp Glu Ala Ile Arg Ala Val
165 170 175

Leu Cys Pro Gln Pro Thr Lys Val Lys Lys Pro Cys Ser Leu Leu 180 185 190

<sup>&</sup>lt;210> 363

<sup>&</sup>lt;211> 1090

<sup>&</sup>lt;212> DNA

<sup>&</sup>lt;213> Schizophyllum commune

<sup>&</sup>lt;220>

<sup>&</sup>lt;221> CDS

<sup>&</sup>lt;222> (145)..(735)

<sup>&</sup>lt;400> 363

gtacccaage cetegeetee eegtegegte gtetgeette tteecetegg ttteegatag	120
tegeteegtt geeeagteee eagt atg eag gee atc aag tgt gtt gte gta Met Gln Ala Ile Lys Cys Val Val Val	171
gga gat ggt gcg gtc gga aag acc tgc ctg cta atc tcg tat acc acg Gly Asp Gly Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Thr 10 15 20 25	219
aac gcg ttc ccg gga gaa tat atc ccg acc gtg ttc gat aac tac tcc Asn Ala Phe Pro Gly Glu Tyr Ile Pro Thr Val Phe Asp Asn Tyr Ser 30 35 40	267
gcc aat gtc atg gtc gac ggc aag act atc tcc ctc ggg ctt tgg gat Ala Asn Val Met Val Asp Gly Lys Thr Ile Ser Leu Gly Leu Trp Asp 45 50 55	315
acc get ggt caa gaa gat tac gac cgt ete ege eeg ete tee tac eet Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro 60 65 70	363
cag acg gat gtc ttc ttg att tgt ttc tcg ctc gtc agc ccg cca agt Gln Thr Asp Val Phe Leu Ile Cys Phe Ser Leu Val Ser Pro Pro Ser 75 80 85	411
ttc gag aac gtc cgg acc aag tgg tac cct gaa ata tcg cat cac gca Phe Glu Asn Val Arg Thr Lys Trp Tyr Pro Glu Ile Ser His His Ala 90 95 100 105	459
ccg cag acg ccc gtc gtg ctc gtg ggc acc aag ctg gat ttg cga gag Pro Gln Thr Pro Val Val Leu Val Gly Thr Lys Leu Asp Leu Arg Glu 110 115	507
gac cct gcg acg ata gag aaa ctg cgt gac cgc cgc atg tcc ccc atc Asp Pro Ala Thr Ile Glu Lys Leu Arg Asp Arg Arg Met Ser Pro Ile 125 130 135	555
cag tac tcg cag ggt gtc gcg atg atg aag gac atc ggt gct gtg aag Gln Tyr Ser Gln Gly Val Ala Met Met Lys Asp Ile Gly Ala Val Lys 140 145 150	603
tac cta gag tgt tcc gcg ctg acg caa aag ggg ctc aag acc gtg ttt Tyr Leu Glu Cys Ser Ala Leu Thr Gln Lys Gly Leu Lys Thr Val Phe 155 160 165	651
gac gag gcg atc cgt gtt gtc ttg tac ccg tcc gcg cgg tcc gac aac Asp Glu Ala Ile Arg Val Val Leu Tyr Pro Ser Ala Arg Ser Asp Asn 170 175 180 185	699
aaa cgc agc aag ggc cgc tca tgc att gtc gca taagtggact ccagcgccgc Lys Arg Ser Lys Gly Arg Ser Cys Ile Val Ala 190	752
tgtatgggtg gacgaaccac aggaagtgtt gtgcgcactg tatcatcacg cggcgcgcgg	812
cgctccctgc actatatcac gccatttatg tctttcttct agcactatct cctttttcgc	872
gccagctgct gatatccgca cggtttcctg ccaacacata ccagtggaac tcgaggatcc	932
. tgaccatttt gctactcgtc acgaccaccc ttgcctcaca ccccctttgt gttgactctc	992
aggttetgta attegaegae etgetetteg aatttegete eeetttgeee acatageaca	1052
tatagtatca ccgtgacgaa ctgtatcctc cttgacga	1090

<sup>&</sup>lt;210> 364 <211> 196 <212> PRT <213> Schizophyllum commune

	0> 3 Gln		Ile	Lys	Cys	Val	. Val	. Val	Gly	Asp	Gly	Ala	Val	Gly	Lys		
1				· 5					10					15	Tyr		
			20					- 25	•				30		_		
		35					40					45		_	Gly		•
Lys	Thr 50	Ile	Ser	Leu	ı Gly	Leu 55	Trp	Asp	Thr	Ala	Gly 60	Gln	Glu	Asp	Tyr		
Asp 65	Arg	Leu	Arg	Pro	Leu 70	Ser	Туг	Pro	Gln	Thr 75		Val	Phe	Leu	Ile 80		
	Phe	Ser	Leu	Val 85	Ser	Pro	Pro	Ser	Phe		Asn	Val	Arg		Lys	•	
Trp	Tyr	Pro	Glu 100		Ser	His	His	Ala 105		Gln	Thr	Pro			Leu		
Val	Gly	Thr 115		Leu	Asp	Leu	Arg	Glu	Asp	Pro	Ala				Lys		
Leu	Arg		Arg	Arg	Met				Gln	Tyr		125 Gln		Val	Ala		
Met		Lvs	Asp	Ile	Gly	135 Ala	val	Lva	Tvr	T.e.11	140	Cva	Sor	. Δ1=	T.e.u		
145					150 Lys		•	•		155			•		160		
				165					170					175			
			180		1119	501	Top	185	цуз	Arg	SET	ъу	190	AIG	ser		
Cys	TTE	Val 195	Ala		•									٠			
	0> 3										•						
	r> 2.														٠		
	2 > D1 3 > P:		occio	dioie	des 1	ora e	ilie	neie		•	:				•		
~		A	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	<u> </u>	ucs .	JIGS.	LLIC	TOTO								, ,	
<220										•							
	L> CI	DS L)(	(576)														
			(376)	,							•						
	)> 36 act		att	cat.	cgt	222	ctt	atc	att	att.	aat	a t	aat	~~~	+~+		40
Met 1	Ala	Glu	Ile	Arg 5	Arg	Lys	Leu	Val	Ile 10	Val	Gly	Asp	Gly	Ala 15	Cys		48
ggt	aaa	act	tgt	ctc	ttg	att	gtc	ttt	tcc	aag	ggt	acc	ttc	cct	gag		96
Gly	ГÄЗ	Thr	Cys 20	Leu	Leu	Ile	Val	Phe 25	Ser	Lys	Gly	Thr	Phe	Pro	Glu		
gtc	tac	gtc	cca.	acc	gtc	ttc	gag	aæc	tat	gtg	gcc	gac	gtt	gag	gtc	-	144
		35			Val		40					45				٠	
gat	gga	aag	cat	gtc	gag	ctc	gca	ctt	tgg	gat	acg	gct	ggc	cag	gaa		192
	50				Glu	55					60		_			٠	
gat	Tur	gat	cga	CCC	aga Arg	CCT	Ctt	tcc	tac	cct	gat	tca	cat	gtt	att		240
65					70					75	_	•			80		
Ctg	atc	tgt	Dho	gct	atc	gat	tcc	CCC	gac	tct	ctc	gac	aac	gtc	cag		288
				85	Ile				90			_		95			
Glu	Lys	Trp	Ile	Ser	gaa Glu	Val	Leu	Cat His	Phe	Cys Cgc	cag Gln	ggt Gly	cat His	Pro	att Ile		336
			100					105					110				
atc Ile	ccc Leu	gtt Val	ggt Glv	tgc Cys	aag Lys	aaa Lys	gat Asp	Ctt	cgt Ara	gac Asp	gac Asp	Pro	aga Arg	acg Thr	att		384
		115					120				•	125				•	
gag	gag	ctg	cgc	aag	acg	tct	cag	aag	ccc	gtg	acc	acc	gaa	cag	ggt		432
Glu	Glu 130	Leu .	Arg	Lys	Thr	Ser 135	Gln	Lys	Pro	Val	Thr 140	Thr	Glu	Gln	Gly		
gag	σaσ	gtc	cac	aao	aaq		aac	act	taci			ata					480
3-3	5-5		-5-		3		22~	9	cac	aug	Lat	ccg	gaa	Lgc	ECC	•	*0U
Glu	Glu	Val /	Arg	Lys	Lys	Ile	Gly	Ala	Tyr	Lys	Tyr	Leu	gaa Glu	Cys	Ser	•	400

145 gcc Ala	cga Arg	aca Thr	Asn	gac Asp	150 gga Gly	gtt Val	cgt Arg	gag Glu	gtg Val	155 ttc Phe	gag Glu	tca Ser	gct Ala	act Thr	160 cga Arg		528
gct Ala	gca Ala	ctg Leu	ctg	gcg	aag Lys	aag Lys	gag Glu	aaa Lys 185	aag Lys	aaa Lys	tgc Cys	aag Lys	atc Ile 190	ttg Leu			573
taa																•	576

<210> 366 <211> 191 <212> PRT <213> Paracoccidioides brasiliensis

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<210> 367 <211> 591 <212> DNA <213> Fucus distichus

<220>
<221> CDS
<222> (1)..(591)

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tgc Cys	ttc Phe	agc Ser	gtc Val	gtt Val 85	gac Asp	ccc Pro	acc Thr	agc Ser	ttt Phe 90	cac His	aac Asn	gtg Val	aag Lys	ctc Leu 95	aag Lys		288
tgg Trp	ata Ile	ccc Pro	gag Glu 100	ctg Leu	caa Gln	cac His	cat His	gct Ala 105	ccg Pro	ggc Gly	atc Ile	cca Pro	ttt Phe 110	ata Ile	ctg Leu		336
gtt Val	ggt Gly	acg Thr 115	aag Lys	ctc Leu	gac Asp	ctg Leu	agg Arg 120	gat Asp	gat Asp	caa Gln	gac Asp	gcg Ala 125	atc Ile	aag Lys	cgt Arg		384
cta Leu	gca Ala 130	gaa Glu	cgt Arg	cgg Arg	cag Gln	acg Thr 135	ccc Pro	atc Ile	agc Ser	ttc Phe	agc Ser 140	gag Glu	gcg Ala	cag Gln	ggt Gly		432
ctg Leu 145	tcg Ser	tct Ser	gac Asp	ctt Leu	gaa Glu 150	gct Ala	tac Tyr	cgc	tac Tyr	ctt Leu 155	gag Glu	tgc Cys	agc Ser	gcg Ala	ctg Leu 160	•	480
acg Thr	caa Gln	cac His	GJA aaa	tta Leu 165	aaa Lys	cag Gln	gtg Val	ttt Phe	gac Asp 170	GJÀ aaa	gct Alạ	atc Ile	cgg Arg	tgt Cys 175	gtt Val		528
cta Leu	gaa Glu	cag Gln	aac Asn 180	cag Gln	aga Arg	aag Lys	atg Met	aaa Lys 185	aag Lys	aaa Lys	aag Lys	ggc Gly	aag Lys 190	aaa Lys	ggc	÷	576
_	_	atc Ile 195	tct Ser	tga													591

<210> 368

<211> 196

<212> PRT .

<213> Fucus distichus

<400> 368

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<210> 369

<211> 636

<212> DNA

<213> Homo sapiens

195

<220>

<221> CDS

<222> (1)..(636).

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atc Ile	cct Pro	act Thr 35	gtc Val	ttt Phe	gac Asp	aat Asn	tat Tyr 40	tct Ser	gcc Ala.	aat Asn	gtt Val	atg Met 45	gta Val	gat Asp	gga Gly	144
Lys	Pro 50	Val	Asn	Leu	Gly	Leu 55	Trp	Asp	Thr	Ala	Gly 60	Gln	Glu	Asp	Tyr	192
gac Asp 65	aga	tta Leu	cgc Arg	ccc Pro	cta Leu 70	tcc Ser	tat Tyr	ccg Pro	caa Gln	aca Thr 75	gtt Val	gga Gly	gaa Glu	acg Thr	tac Tyr 80	240
ggt Gly	aag Lys	gat Asp	ata Ile	acc Thr 85	tcc Ser	cgg Arg	Gly	aaa Lys	gac Asp 90	aag Lys	ccg Pro	att Ile	gcc	gat Asp 95	gtg Val	288
ttc Phe	tta Leu	att Ile	tgc Cys 100	ttt Phe	tcc Ser	ctt Leu	gtg Val	agt Ser 105	cct Pro	gca Ala	tca Ser	ttt Phe	gaa Glu 110	aat Asn	gtc Val	336
cgt Arg	gca Ala	aag Lys 115	tgg	tat Tyr	cct Pro	gag Glu	gtg Val 120	cgg Arg	cac His	cac His	tgt Cys	CCC Pro 125	aac Asn	act Thr	ccc Pro	384
atc Ile	atc Ile 130	cta	gtg Val	gga Gly	act Thr	aaa Lys 135	ctt	gat Asp	ctt Leu	agg Arg	gat Asp 140	gat Asp	aaa Lys	gac Asp	acg Thr	432
atc Ile 145	gag	aaa Lys	ctg Leu	aag Lys	gag Glu 150	aag Lys	aag Lys	ctg Leu	act Thr	ccc Pro 155	atc Ile	acc Thr	tat Tyr	ccg Pro	cag Gln 160	480
aat	cta Leu	gcc Ala	atg Met	gct Ala 165	aag Lys	gag Glu	att Ile	ggt Gly	gct Ala 170	gta Val	aaa Lys	tac Tyr	ctg Leu	gag Glu 175	tgc Cys	528
tcg Ser	gcg Ala	ctc Leu	aca Thr 180	cag Gln	cga Arg	Gly	ctc Leu	aag Lys 185	aca Thr	gtg Val	ttt Phe	gac Asp	gaa Glu 190	gcg Ala	atc Ile	576
cga Arg	gca Ala	gtc Val 195	ctc Leu	tgc Cys	ccg Pro	cct Pro	ccc Pro 200	Val	aag Lys	aag Lys	agg Arg	aag Lys 205	aga Arg	aaa Lys	tgc Cys	624
	ctg Leu 210	ttg	taa													636

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<213> Homo sapiens

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<b>-7</b> -2	130					135					140						•
11e	GIU	гу	Leu	гъхв	150		Lys	Leu	Thr			Thr	Туг	Pro	Gln		
		Ala	Met	Ala	Lys		Ile	Glv	· Ala	155 Val		Tvr	Let	(G1)	160 Cvs		
				165	i				170					175			
			180					185			. •		190	)	Ile		
Arg	Ala	Val	Leu	Cys	Pro	Pro			Lys	Lys	Arg			Lys	Cys		
Leu	Leu	195 Leu					200		•			205					
	210		-							٠.		×			•		
-01							-										
	0 > 3° 1 > 5°													•			
	2> D																
<21	3 > P	neum	ocys	tis	cari	nii	•										·
<22	n s																
	1> C	DS											•				
<22	2> (:	1)	(576	)			•										
-401	0> 3'	71															
			att	aaa	tgt	gtc	qtt	qtt	aaa	gat	ggc	aca	att	aat.	aaa		48
Met	Gln	Thr	Ile	Lys	Cys	Val	Val	Val	Gly	Asp	Ğİy	Ala	Val	Gly	Lys		
1	tat	att	++=	5 ===	taa	++	200	2.62	10		سند			15			
Thr	Cys	Leu	Leu	Ile	tcc Ser	Tyr	Thr	Thr	Asn	Lvs	Phe	Pro	Ser	Glu	Tur		96
			20					25					30				
gtt	cct	act	gta	ttt	gat	aat	tat	gcg	gtt	acc	gta	atg	att	gga	gaa		144
vaı	PIO	35	Val	PHE	Asp	ASII	17r	Ата	vaı	Thr	Agri	Met 45	IFe	GTA	Glu	•	
gaa	cct	tat	act	tta	gga	ctt	ttt	gat	aca	gca	ggt	caa	gaa	gat	tat		192
Glu	Pro	Tyr	Thr	Leu	Gly	Leu	Phe	Asp	Thr	Ala	Gly	Gln	Glu	Asp	Tyr		
gac	50 aga	tta	cat	ccc	tta	55 t.ca	tat	cca	саа	aca	60 gat	att	+++	ctt	a++		240
Asp	Arg	Leu	Arg	Pro	Leu	Ser	Tyr	Pro	Gln	Thr	Asp	Val	Phe	Leu	Ile		240
65			-		70					75	-				80		
Cvs	Phe	Ser	gcc Val	act Thr	agt Ser	CCA	gca	agt	Dhe	gaa	aat	gta	aga	gaa	aag		288
<b>0</b> 10			•	85			ALα	BCI.	90	Giu	MSII	vaı	Arg	95	пĀг		
tgg	cat	cca	gag	gtt	cgt	cat	cat	tgt	cca	gga	aca	CCC	tgt	ctt	att		336
Trp	Hls	Pro	100	Val	Arg	His	His	Cys 105		Gly	Thr	Pro		Leu	Ile		
gtt	ggt	aca		atc	gat	tta	cqa			cct	ato	att	110 gta	gag	aaa		384
Val	ĞĨy	Thr	Gln	Ile	Asp	Leu	Arg	Āsp	Āsp	Pro	Met	Ile	Val	Glu	Lys		
ctc	= a+	115	<b>.</b>	202	<b>G</b> 2.3	2.66	120					125				•	
Leu	Ser	Arg	Gln	Arg	caa Gln	Thr	Pro	Ile	Thr	Lvs	Glu	Leu	Glv	Glu	Lvs		432
	130	•				135					140		_		-		
Ctt	tca	aaa	gaa	ttg	ggt	gct	gta	aaa	tat	gtt	gag	tgc	tca	gct	ttg		480
145	ser	цуз	GIU	neu	Gly 150	ALA	val	гÀг	TYF	155	GIU	Cys	ser	ATA	ьец 160		
act	caa	aaa	gga	tta	aaa	aac	gtt	ttt	gat	gaa	gct	ata	gtt	tgc	qca		528
Thr	Glņ	Lys	Gly	Leu	Lys	Asn	Val	Phe	Asp	Glu	Ala	Ile	Val	Cys	Ala		, .
ctt	σaa	cca	ccc	165 gtt	acg	aad.	aaci	aaa	170 act	222	tat	ctt	att	175			573
Leu	Glu	Pro	Pro	Val	Thr	Lys	Lys	Lys	Thr	Lys	Cys	Leu	Ile	Leu			5/3
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taa												. •					576

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Val Pro Thr Val Phe Asp Asn Tyr Ala Val Thr Val Met Ile Gly Glu
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Glu Pro Tyr Thr Leu Gly Leu Phe Asp Thr Ala Gly Gln Glu Asp Tyr
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Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Ile
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                                           75
Cys Phe Ser Val Thr Ser Pro Ala Ser Phe Glu Asn Val Arg Glu Lys
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Trp His Pro Glu Val Arg His His Cys Pro Gly Thr Pro Cys Leu Ile
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Val Gly Thr Gln Ile Asp Leu Arg Asp Asp Pro Met Ile Val Glu Lys
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Leu Ser Arg Gln Arg Gln Thr Pro Ile Thr Lys Glu Leu Gly Glu Lys
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 ggc gac ggg gcg tgt ggg aag acg tgt ctg ctc gtt gtg ttc tcc aaa
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Gly Asp Gly Ala Cys Gly Lys Thr Cys Leu Leu Val Val Phe Ser Lys
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ggg cag ttc ccg gag atc cat gtg ccc acg gtg ttc gag aac tac gtg
Gly Gln Phe Pro Glu Ile His Val Pro Thr Val Phe Glu Asn Tyr Val
                                                                            144
                                                    45
                              40
                                                                            192
 gca gat gtg gac atc gac ggg cga cgc gta gag ctg gca ctg tgg gat
 Ala Asp Val Asp Ile Asp Gly Arg Arg Val Glu Leu Ala Leu Trp Asp
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 aca gcg ggc cag gag gac tac gac cgg ctg cgg cca ttg tcg tac ccg
                                                                            240
 Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro
                      70
 gat tee aat gtg gtg ett ate tgt tte tet gtg gae eta eet gae teg
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 Asp Ser Asn Val Val Leu Ile Cys Phe Ser Val Asp Leu Pro Asp Ser
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                                      90
                  85
 ctg gac aat gtg cag gag aag tgg gtc agc gaa gtt ctg cac ttc tgc
                                                                            336
 Leu Asp Asn Val Gln Glu Lys Trp Val Ser Glu Val Leu His Phe Cys
                                                         110
              100
                                   105
 cag ggc gtg cca att tta ctg gta ggc tgc aag gtg gat ctg aga aac Gln Gly Val Pro Ile Leu Leu Val Gly Cys Lys Val Asp Leu Arg Asn
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                                                    125
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 Asp Pro Gln Val Leu Gln Gln Leu Gln Ala Glu Gly Gln Arg Pro Val
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                                                140
 acc gcc gca gag ggc tca gcc gtc gcc ggt aag ata ggc gcc gtc gcc
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 Thr Ala Ala Glu Gly Ser Ala Val Ala Gly Lys Ile Gly Ala Val Ala
                                                                 160
                                            155
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 tac ctc gag tgc tct gcg cgc aca ggc cag ggt gtg aag gag gtt ttc
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 Tyr Leu Glu Cys Ser Ala Arg Thr Gly Gln Gly Val Lys Glu Val Phe
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180		gac	act	gcg	aco	: cgc	geo	gea	cto	tet	qq	aad		e ge	ges	t te	r gca		576
Ctg tga  Ctg  Ctg  Ctg  Ctg  Ctg  Ctg  Ctg	•				180	)				185	i				190	)			
Californ   Californ		Gly	aag Lys	Lys	Lys	gto Val	: cac His	ggt Gly	/ Asr	Lys	Lys	g aag	g aag s Lys	Lys	Cys	cto	g gtc ı Val		624
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Met Ala Tyr Gln Thr Gly Gly Asn Ile Arg Lys Lys Leu Val Ile Val  Gly Asp Gly Ala Cys Gly Lys Thr Cys Leu Leu Val Val Phe Ser Lys 20  Gly Gln Phe Pro Glu Ile His Val 35  Ala Asp Val Asp Ile Asp Gly Arg Arg Val Glu Leu Ala Leu Trp Asp 50  Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro 65  Asp Ser Asn Val Val Leu Ile Cys Phe Ser Val Asp Leu Pro Asp Ser 85  Leu Asp Asn Val Glu Lys Trp Val Ser Glu Val Leu His Phe Cys 100  Gln Gly Val Glu Leu Leu Val Gly Cys Lys Val Asp Leu Arg Asn 115  Asp Pro Gln Val Leu Gln Gln Leu Gln Ala Glu Gly Gln Arg Pro Val 130  Thr Ala Ala Glu Gly Ser Ala Val Ala Gly Lys Ile Gly Ala Val Ala 145  Tyr Leu Glu Cys Ser Ala Arg Thr Gly Gln Gly Val Lys Glu Val Phe 165  Asp Thr Ala Thr Arg Ala Ala Leu Ser Gly Lys Pro Ala Ala Ser Ala 180  Gly Lys Lys Lys Val His Gly Asp Lys Lys Lys Lys Gys Leu Val 195  Leu     210  221  220  221  220  221  222  (21)  375  422  222  (21)  564  221  222  (21)  576  Ala Cys Gly lys Thr Ser Leu Leu His Sval Phe Thr Leu Gly Lys Phe 20  20  221  220  220  221  220  221  220  220  221  220  221  220  221  220  222  225  231  240  248  Ala Cys Gly lys Thr Ser Leu Leu His Val Phe Thr Leu Gly Lys Phe 20  225  226  227  227  228  229  227  229  227  229  229		<21	3> A	shby	a go	ssyp	ii											-	
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20		1 .				5					10				•	. 15			.:
Ala Asp Val Asp Ile Asp Gly Arg Arg Val Glu Leu Ala Leu Trp Asp 50 Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro 65 Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro 75 80 Asp Ser Asn Val Val Leu Ile Cys Phe Ser Val Asp Leu Pro Asp Ser 85 Leu Asp Asn Val Gln Glu Lys Trp Val Ser Glu Val Leu His Phe Cys 100 Gln Gly Val Pro Ile Leu Leu Val Gly Cys Lys Val Asp Leu Arg Asn 115 Asp Pro Gln Val Leu Gln Gln Leu Gln Ala Glu Gly Gln Arg Pro Val 130 135 Thr Ala Ala Glu Gly Ser Ala Val Ala Gly Lys Ile Gly Ala Val Ala 145 Tyr Leu Glu Cys Ser Ala Val Ala Gly Lys Ile Gly Ala Val Ala 150 Tyr Leu Glu Cys Ser Ala Yal Arg Thr Gly Gln Gly Val Lys Glu Val Phe 165 Asp Thr Ala Thr Arg Ala Ala Leu Ser Gly Lys Pro Ala Ala Ser Ala 180 Gly Lys Lys Lys Val His Gly Asp Lys Lys Lys Lys Cys Leu Val 195 Leu <a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a< td=""><td></td><td></td><td></td><td></td><td>20</td><td></td><td></td><td></td><td></td><td>25</td><td></td><td></td><td></td><td></td><td>30</td><td>٠.</td><td></td><td>•</td><td></td></a<></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a>					20					25					30	٠.		•	
50. 55 Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro 65 Thr Ala Gly Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro 65 Asp Ser Asn Val Val Leu Ile Cys Phe Ser Val Asp Leu Pro Asp Ser 85 Leu Asp Asn Val Gln Glu Lys Trp Val Ser Glu Val Leu His Phe Cys 100 Gln Gly Val Pro Ile Leu Leu Val Gly Cys Lys Val Asp Leu Arg Asn 115 Asp Pro Gln Val Leu Gln Gln Leu Gln Ala Glu Gly Gln Arg Pro Val 130 Thr Ala Ala Glu Gly Ser Ala Val Ala Gly Lys Ile Gly Ala Val Ala 145 Tyr Leu Glu Cys Ser Ala Arg Thr Gly Gln Gly Val Lys Glu Val Phe 160 Tyr Leu Glu Cys Ser Ala Arg Thr Gly Gln Gly Val Lys Glu Val Phe 161 Asp Thr Ala Thr Arg Ala Ala Leu Ser Gly Lys Pro Ala Ala Ser Ala 180 Gly Lys Lys Lys Val His Gly Asp Lys Lys Lys Lys Cys Leu Val 195 Leu <a href="#"></a>				35			•		40					45		_			
Asp Ser Asn Val Val Leu Ile Cys Phe Ser Val Asp Leu Pro Asp Ser 85			50					55					60.			_	_		
Asp Ser Asn Val Val Leu Ile Cys Phe Ser Val Asp Leu Pro Asp Ser 85  Leu Asp Asn Val Gln Glu Lys Trp Val Ser Glu Val Leu His Phe Cys 100  Gln Gly Val Pro Ile Leu Leu Val Gly Cys Lys Val Asp Leu Arg Asn 115  Asp Pro Gln Val Leu Gln Gln Leu Gln Ala Glu Gly Gln Arg Pro Val 130  Thr Ala Ala Glu Gly Ser Ala Val Ala Gly Lys Ile Gly Ala Val Ala 160  Tyr Leu Glu Cys Ser Ala Arg Thr Gly Gln Gly Val Lys Glu Val Phe 175  Asp Thr Ala Thr Arg Ala Ala Leu Ser Gly Lys Pro Ala Ala Ser Ala 180  Gly Lys Lys Lys Val His Gly Asp Lys Lys Lys Lys Cys Leu Val 195  Leu   **210> 375  <221> 205  **222> (1)(564)**  **400> 375  atg acg gtc aac gtt gtg aga cgg aag ttg gta atc ata ggg gat ggg 48  Met Thr Val Asn Val Val Arg Arg Lys Leu Val Ile Ile Gly Asp Gly 1  gca tgc ggc aag acg tcg ta cta cat gtg gta atc ata ggg gat ggg 48  Ash Cys Gly Lys Thr Ser Leu Leu His Val Phe Thr Leu Gly Lys Phe 20  Cct gag gaa tat ctg ccc acg gtt ttc gag aac tac gtt acg gat acg 144  Pro Glu Glu Tyr Leu Pro Thr Val Phe Glu Asn Tyr Val Thr Asp Cys 45  Cgt gta gac ggc at aca gtt gcg at ttg gcd ta gct gct gtt acc 192  Cgt gta gac ggc at aca gtt gcg at ttg gcd at acc act gct gct acc gct gcd ta 62  Cgt gta gac ag act gcd ta aca gtt gcg at ttg gad act acc gct gcd tacc acc gct gcd tacc acc gct ttg gad acc tac gct gcd tacc acc gct ttg gad acc tac gad ttc gcd gad tacc acc gct gcd tacc acc gct ttg gad acc tac gcd gad tacc gcd gcd tacc acc gcd gcd tacc acc gcd ttg gcd cac gcd gcd tacc acc gcd ttg gcd cac gcd ttg gcd cac gcd gcd tacc acc gcd ttg gcd cac gcd gcd tacc acc gcd ttg gcd cac gcd gcd tacc acc gcd ttg gcd cac gcd gcd tacc acc gcd ttg gcd cac gcd gcd gcd gcd gcd gcd gcd gcd gcd gc		Thr 65	Ala	Gly	Gln	Glu		Tyr	Asp	Arg	Leu		Pro	Leu	Ser	Tyr			
Leu Asp Asn Val Gln Glu Lys Trp Val Ser Glu Val Leu His Phe Cys 100 Gln Gly Val Pro Ile Leu Leu Val Gly Cys Lys Val Asp Leu Arg Asn 115 120 Asp Pro Gln Val Leu Gln Gln Leu Gln Ala Glu Gly Gln Arg Pro Val 130 Thr Ala Ala Glu Gly Ser Ala Val Ala Gly Lys Ile Gly Ala Val Ala 145 Tyr Leu Glu Cys Ser Ala Arg Thr Gly Gln Gly Val Lys Glu Val Phe 165 170 Asp Thr Ala Thr Arg Ala Ala Leu Ser Gly Lys Pro Ala Ala Ser Ala 180 Gly Lys Lys Lys Lys Val His Gly Asp Lys Lys Lys Lys Cys Leu Val 195 Leu <a href="#"></a>		Asp	Ser	Asn	Val		Leu	Ile	Сув	Phe		Val	Asp	Leu	Pro		Ser	•	
Gln Gly Val Pro Ile Leu Leu Val Gly Cys Lys Val Asp Leu Arg Asn 115 125  Asp Pro Gln Val Leu Gln Gln Leu Gln Ala Glu Gly Gln Arg Pro Val 130 135 140  Thr Ala Ala Glu Gly Ser Ala Val Ala Gly Lys Ile Gly Ala Val Ala 145 150 155 160  Tyr Leu Glu Cys Ser Ala Arg Thr Gly Gln Gly Val Lys Glu Val Phe 175 175  Asp Thr Ala Thr Arg Ala Ala Leu Ser Gly Lys Pro Ala Ala Ser Ala 180 185 190  Gly Lys Lys Lys Val His Gly Asp Lys Lys Lys Lys Lys Cys Leu Val 195 200  Leu <pre> </pre> <a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a href="#"><a #"="" href="#&lt;/td&gt;&lt;td&gt;&lt;/td&gt;&lt;td&gt;Leu&lt;/td&gt;&lt;td&gt;Asp&lt;/td&gt;&lt;td&gt;Asn&lt;/td&gt;&lt;td&gt;Val&lt;/td&gt;&lt;td&gt;&lt;/td&gt;&lt;td&gt;Glu&lt;/td&gt;&lt;td&gt;Lys&lt;/td&gt;&lt;td&gt;Trp&lt;/td&gt;&lt;td&gt;&lt;/td&gt;&lt;td&gt;Ser&lt;/td&gt;&lt;td&gt;Glu&lt;/td&gt;&lt;td&gt;Val&lt;/td&gt;&lt;td&gt;Leu&lt;/td&gt;&lt;td&gt;&lt;/td&gt;&lt;td&gt;Phe&lt;/td&gt;&lt;td&gt;Суз&lt;/td&gt;&lt;td&gt;&lt;/td&gt;&lt;td&gt;· .&lt;/td&gt;&lt;/tr&gt;&lt;tr&gt;&lt;td&gt;Asp Pro Gln Val Leu Gln Gln Leu Gln Ala Glu Gly Gln Arg Pro Val  130  135  Thr Ala Ala Glu Gly Ser Ala Val Ala Gly Lys Ile Gly Ala Val Ala  145  Tyr Leu Glu Cys Ser Ala Arg Thr Gly Gln Gly Val Lys Glu Val Phe  165  Asp Thr Ala Thr Arg Ala Ala Leu Ser Gly Lys Pro Ala Ala Ser Ala  180  Gly Lys Lys Lys Val His Gly Asp Lys Lys Lys Lys Cys Leu Val  195  Leu   &lt;pre&gt; &lt;/pre&gt;  &lt;a href="> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="#"> <a href="&lt;/td"><td></td><td>Gln</td><td>Gly</td><td>Val</td><td></td><td>Ile</td><td>Leu</td><td>Leu</td><td></td><td></td><td>Cys</td><td>Lys</td><td>.Val</td><td></td><td>Leu</td><td>Arg</td><td>Asn</td><td></td><td>•</td></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a></a>		Gln	Gly	Val		Ile	Leu	Leu			Cys	Lys	.Val		Leu	Arg	Asn		•
Thr Ala Ala Glu Gly Ser Ala Val Ala Gly Lys Ile Gly Ala Val Ala  150  150  150  150  177  Leu Glu Cys Ser Ala Arg Thr Gly Gln Gly Val Lys Glu Val Phe  165  170  175  Asp Thr Ala Thr Arg Ala Ala Leu Ser Gly Lys Pro Ala Ala Ser Ala  180  180  Gly Lys Lys Lys Lys Lys Lys Lys Cys Leu Val  195  Leu   C210> 375  <221> 564  <212> DNA  <2213> Ashbya gossypii  <220> <222> (1)(564)  <400> 375  atg acg gtc aac gtt gtg aga cgg aag ttg gta atc ata ggg gat ggg Met Thr Val Asn Val Val Arg Arg Lys Leu Val Ile Ile Gly Asp Gly  1  gca tgc ggc aag acg tcg tta cta cat gtg ttc acg ctg ggg aag ttc Ala Cys Gly Lys Thr Ser Leu Leu His Val Phe Thr Leu Gly Lys Phe  20  cct gag gaa tat ctg ccc acg gtt ttc gag aac tac gtt acg gat tgc Pro Glu Glu Tyr Leu Pro Thr Val Phe Glu Asn Tyr Val Thr Asp Cys  20  cgt gta gac ggc ata aac gtt gcg cta tog gag at act gct ggt  22  cgt gta gac ggc ata aac gtt gcg cta tog cta tog gat act gct ggt  23  cgt gta gac ggc ata aac gtt gcg cta tag gat ttg gca cta tog gat act gct ggt  144  Pro Glu Glu Tyr Leu Pro Thr Val Phe Glu Asn Tyr Val Thr Asp Cys  25  cgt gta gac ggc ata aac gcg cat tag cta tag gat act gct ggt  26  cgt gta gac ggc ata aac gct cg tta cta tag gat tag cga tag cgg gat acg cgg gat acg ttg cat tag gat act gct ggt  182  183  184  185  186  190  185  190  185  190  185  185  190  185  186  190  187  188  189  189  189  189  189  189		Asp	Pro		Val	Leu	Gln			Gln	Ala	Glu		Gln	Arg	Pro	Val		
Tyr Leu Glu Cys Ser Ala Arg Thr Gly Gln Gly Val Lys Glu Val Phe  165  170  175  Asp Thr Ala Thr Arg Ala Ala Leu Ser Gly Lys Pro Ala Ala Ser Ala  180  180  Gly Lys Lys Lys Lys Val His Gly Asp Lys Lys Lys Lys Lys Cys Leu Val  195  Leu <pre> </pre> <pre> <pre> </pre> <pre> </pre>  200  Leu  <pre> </pre>  210&gt; 375 </pre> <pre> &lt;211&gt; 564 </pre> <pre> &lt;2212&gt; DNA </pre> <pre> &lt;2213&gt; Ashbya gossypii</pre> <pre> <pre> <pre> <pre> &lt;220&gt; &lt;221&gt; CDS </pre> <pre> &lt;221&gt; CDS </pre> <pre> &lt;222&gt; (1)(564) </pre> <pre> =""><td></td><td>Thr</td><td></td><td>Ala</td><td>Glu</td><td>Gly</td><td>Ser</td><td></td><td>Val</td><td>Ala</td><td>Gly</td><td></td><td></td><td>Gly</td><td>Ala</td><td>Val</td><td>Ala</td><td></td><td></td></p<></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre>		Thr		Ala	Glu	Gly	Ser		Val	Ala	Gly			Gly	Ala	Val	Ala		
Asp Thr Ala Thr Arg Ala Ala Leu Ser Gly Lys Pro Ala Ala Ser Ala 180 185 190 Gly Lys Lys Lys Val His Gly Asp Lys Lys Lys Lys Cys Leu Val 195 200 205 Leu <pre> <a href="#">200</a> 205 Leu  <pre> <a href="#">201</a> 205 Leu </pre>  <pre> <a href="#">201</a> 205 Leu </pre>   210 &gt; 375 <a href="#">2211 &gt; 564</a> <a href="#">2212 &gt; DNA</a> <a href="#">2213 &gt; Ashbya gossypii</a> <a href="#">2220 &gt; (221 &gt; CDS</a> <a href="#">2222 &gt; (1) (564)</a> <a href="#">400 &gt; 375</a> atg acg gtc aac gtt gtg aga cgg aag ttg gta atc ata ggg gat ggg Met Thr Val Asn Val Val Arg Arg Lys Leu Val Ile Ile Gly Asp Gly 1 5 Gca tgc ggc aag acg tcg tta cta cat gtg ttc acg ctg ggg aag ttc Ala Cys Gly Lys Thr Ser Leu Leu His Val Phe Thr Leu Gly Lys Phe 20 Cct gag gaa tat ctg ccc acg gtt ttc gag aac tac gtt acg gat tgc Pro Glu Glu Tyr Leu Pro Thr Val Phe Glu Asn Tyr Val Thr Asp Cys 35 Cgt gta gac ggc ata aac gtg cag ttg gcg cta tgg gat act act gct ggt 142 Cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat act gct ggr 142 Cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat act gct gcg 142 Cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat act gct gct 142 Cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat act gct gct 142 Cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat act gct gct 142 Cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat act gct gct 142 Cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat act gct gct 142 Cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat act gct gct 142 Cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat ggc gcg cta tgc 143 Cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat act gct gct 144 Cgt gta gac ggc ata aaa aaa gtg cag ttg gcg cta tgg gat ggc gcg cta tgc 144 Cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat ggc gcg gcg gcg gcg gcg gcg gcg gcg gc</pre>			Leu	Glu	Cys	Ser		Arg	Thr	Gly	Gln		Val	Lys	Glu	Val	160 Phe		
Gly Lys Lys Lys Val His Gly Asp Lys Lys Lys Lys Lys Cys Leu Val  195 200 205  Leu <pre> <pre> <pre> <pre> </pre> </pre> <pre> /pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre></pre>		Asp	Thr	Ala	Thr		Ala	Ala	Leu	Ser	170 Gly	Lys	Pro	Ala	Ala	175 Ser	Ala		
Leu  200 205  Leu  200 205  Leu  200  205  Leu  200  210					180					185					190				
<pre>&lt;211&gt; 564 &lt;212&gt; DNA &lt;213&gt; Ashbya gossypii  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; (1)(564)  &lt;400&gt; 375 atg acg gtc aac gtt gtg aga cgg aag ttg gta atc ata ggg gat ggg Met Thr Val Asn Val Val Arg Arg Lys Leu Val Ile Ile Gly Asp Gly 1</pre>		_		195							•				-2-				
<pre>&lt;211&gt; 564 &lt;212&gt; DNA &lt;213&gt; Ashbya gossypii  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; (1)(564)  &lt;400&gt; 375 atg acg gtc aac gtt gtg aga cgg aag ttg gta atc ata ggg gat ggg Met Thr Val Asn Val Val Arg Arg Lys Leu Val Ile Ile Gly Asp Gly 1</pre>		•																	
<pre>&lt;212&gt; DNA &lt;213&gt; Ashbya gossypii  &lt;220&gt; &lt;221&gt; CDS &lt;222&gt; (1)(564)  &lt;400&gt; 375 atg acg gtc aac gtt gtg aga cgg aag ttg gta atc ata ggg gat ggg Met Thr Val Asn Val Val Arg Arg Lys Leu Val Ile Ile Gly Asp Gly 1</pre>																٠.			
<pre>&lt;220&gt; &lt;221&gt; CDS &lt;222&gt; (1)(564)  &lt;400&gt; 375 atg acg gtc aac gtt gtg aga cgg aag ttg gta atc ata ggg gat ggg Met Thr Val Asn Val Val Arg Arg Lys Leu Val Ile Ile Gly Asp Gly 1</pre>		<212	> DN	A.		·				•									
<pre>&lt;221&gt; CDS &lt;222&gt; (1)(564)  &lt;400&gt; 375 atg acg gtc aac gtt gtg aga cgg aag ttg gta atc ata ggg gat ggg Met Thr Val Asn Val Val Arg Arg Lys Leu Val Ile Ile Gly Asp Gly 1</pre>				шоўе	gos	sypı	.1												•
<pre>&lt;400&gt; 375 atg acg gtc aac gtt gtg aga cgg aag ttg gta atc ata ggg gat ggg Met Thr Val Asn Val Val Arg Arg Lys Leu Val Ile Ile Gly Asp Gly 1</pre>		<221	> CD						٠										
atg acg gtc aac gtt gtg aga cgg aag ttg gta atc ata ggg gat ggg  Met Thr Val Asn Val Val Arg Arg Lys Leu Val Ile Ile Gly Asp Gly  1 5 10 15  gca tgc ggc aag acg tcg tta cta cat gtg ttc acg ctg ggg aag ttc  Ala Cys Gly Lys Thr Ser Leu Leu His Val Phe Thr Leu Gly Lys Phe  20 25 30  cct gag gaa tat ctg ccc acg gtt ttc gag aac tac gtt acg gat tgc  Pro Glu Glu Tyr Leu Pro Thr Val Phe Glu Asn Tyr Val Thr Asp Cys  35 40  cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat act gct ggt		<222	> (1	) (	564)					•									
Met Thr Val Asn Val Val Arg Arg Lys Leu Val Ile Ile Gly Asp Gly  1 5 10 15  gca tgc ggc aag acg tcg tta cta cat gtg ttc acg ctg ggg aag ttc 96  Ala Cys Gly Lys Thr Ser Leu Leu His Val Phe Thr Leu Gly Lys Phe 20 25 30  cct gag gaa tat ctg ccc acg gtt ttc gag aac tac gtt acg gat tgc 144  Pro Glu Glu Tyr Leu Pro Thr Val Phe Glu Asn Tyr Val Thr Asp Cys 35 40 45  cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat act gcf ggt 192					aac	qtt	ata	aga	caa	aaσ	tta	gta	atc	ata	aaa '	aat	aaa		40
gca tgc ggc aag acg tcg tta cta cat gtg ttc acg ctg ggg aag ttc Ala Cys Gly Lys Thr Ser Leu Leu His Val Phe Thr Leu Gly Lys Phe 20 25 30  cct gag gaa tat ctg ccc acg gtt ttc gag aac tac gtt acg gat tgc Pro Glu Glu Tyr Leu Pro Thr Val Phe Glu Asn Tyr Val Thr Asp Cys 35 40  cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat act gcf ggt 193		Met	Thr	Val	Asn	Val 5	vai	Arg	Arg	Lys	Leu	Val	Ile	Ile	Gly	Asp	GJÀ		. 40
20 25 30  cct gag gaa tat ctg ccc acg gtt ttc gag aac tac gtt acg gat tgc 144  Pro Glu Glu Tyr Leu Pro Thr Val Phe Glu Asn Tyr Val Thr Asp Cys 35 40 45  cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat act gcr ggt 193		gca Ala	tgc Cvs	ggc Glv	aag	acg	tcg	tta	cta	cat	qtq	ttc	acg	ctg	999	ааσ	ttc		96
Pro Glu Glu Tyr Leu Pro Thr Val Phe Glu Asn Tyr Val Thr Asp Cys  35  40  45  cgt gta gac ggc ata aaa qtg cag ttg gcg cta tgg gat act gcr ggr 192		•			20					25					30				
cgt gta gac ggc ata aaa gtg cag ttg gcg cta tgg gat act gct ggt		Pro	Glu	Glu	Tyr	Leu	Pro	Thr	Val	Phe	gag Glu	aac Asn	tac Tyr	Val	acg Thr	gat Asp	tgc Cys	,	144
Arg val Asp Gly Ile Lys Val Gln Leu Ala Leu Trp Asp Thr Ala Gly		cgt	gta	gac	ggc	ata	aaa	gtg	caq	ttg	gcg	cta	tgg	gat	act	gct	ggt ·		192
		Arg '	val .	Asp	Gly	Ile	Lys	Val	Gln	Leu .	Ala	Leu	Trp	Asp	Thr	Ala	Gly		

	50					55					60					
cag Gln 65	gaa Glu	gaa Glu	tac Tyr	gag Glu	cgt Arg 70	ctg Leu	cgc Arg	ccc Pro	atg Met	tcc Ser 75	tac Tyr	tcg Ser	aag Lys	gcg Ala	gac Asp 80	240
atc Ile	Ile	Leu	Ile	Gly 85	Phe	Ala	Ile	Asp	Asp 90	Pro	Gly ggg	Ser	Leu	Ser 95	Asn	288
gcg Ala	cgg Arg	gag Glu	aag Lys 100	tgg Trp	acg Thr	gtc Val	gag Glu	gcg Ala 105	ctg Leu	cgc Arg	tac Tyr	tgt Cys	CCC Pro 110	aac Asn	gcc	336
ccg Pro	atc Ile	atc Ile 115	ctc Leu	gtg Val	gjå aaa	ctc Leu	aaa Lys 120	aag Lys	gac Asp	ctt Leu	cgc Arg	cgc Arg 125	ccc Pro	Gly ggg	acg Thr	384
cag Gln	tgc Cys 130	gcg Ala	atg Met	gta Val	gcg Ala	cct Pro 135	tcg Ser	cag Gln	gca Ala	caa Gln	gag Glu 140	gtg Val	gtg Val	cgc Arg	gcc Ala	432
atc Ile 145	Gly	gca `Ala	aag Lys	aaa Lys	tac Tyr 150	atg Met	gag Glu	tgc Cys	agc Ser	gca Ala 155	ctt Leu	acg Thr	gjå aaa	gạg Glu	ggç Gly 160	480
gtg Val	gac Asp	gat Asp	gtg Val	ttc Phe 165	gag Glu	ctg Leu	gcc Ala	acg Thr	aga Arg 170	aca Thr	agt Ser	ctt Leu	ctg Leu	gtg Val 175	aac Asn	528
aag Lys	gag Glu	ccg Pro	ggt Gly 180	caa Gln	ggc	tgt Cys	tgc Cys	att Ile 185	atc Ile	tca Ser	tga					 564

<210> 376 <211> 187 <212> PRT <213> Ashbya gossypii

<400> 376 Met Thr Val Asn Val Val Arg Arg Lys Leu Val Ile Ile Gly Asp Gly 10 Ala Cys Gly Lys Thr Ser Leu Leu His Val Phe Thr Leu Gly Lys Phe 30 20 25 Pro Glu Glu Tyr Leu Pro Thr Val Phe Glu Asn Tyr Val Thr Asp Cys 40 35 Arg Val Asp Gly Ile Lys Val Gln Leu Ala Leu Trp Asp Thr Ala Gly 55 Gln Glu Glu Tyr Glu Arg Leu Arg Pro Met Ser Tyr Ser Lys Ala Asp 75 Ile Ile Leu Ile Gly Phe Ala Ile Asp Asp Pro Gly Ser Leu Ser Asn 90 85 Ala Arg Glu Lys Trp Thr Val Glu Ala Leu Arg Tyr Cys Pro Asn Ala 110 105 100 Pro Ile Ile Leu Val Gly Leu Lys Lys Asp Leu Arg Arg Pro Gly Thr 125 120 Gln Cys Ala Met Val Ala Pro Ser Gln Ala Gln Glu Val Val Arg Ala 140 135 130 Ile Gly Ala Lys Lys Tyr Met Glu Cys Ser Ala Leu Thr Gly Glu Gly

155 150 Val Asp Asp Val Phe Glu Leu Ala Thr Arg Thr Ser Leu Leu Val Asn 170 165 Lys Glu Pro Gly Gln Gly Cys Cys Ile Ile Ser

180

<210> 377 <211> 1043 <212> DNA <213> Tigriopus japonicus

<220> <221> CDS <222> (264)..(842)

<400> 377

agg	agga	gac	gcct	tgtt	tg a	aatc	cațc	c aa	caac	ctgg	gac	tctc	tgc	tcca	gcagc	a <sup>.</sup>	60
agc	atca	cca	cccc	catc	ac c	atca	tett	c at	cctg	atca	aca	ccct	tga	gatc	cagat	c ·	120
ccc	atcc	atc	gatc	cacc	ca t	cctg	agga	t tg	actc	acac	acc	tcga	aga	ttgt	gggct	g .	180
tga	aaaa	cca	gtgt	ggga	tc g	gccc.	ttgc	g tg	cgtg	aggt	9991	tggt	tgt	tgaa	acccg	a a	240
ctg	gcçt	gac	catt	gtcg	tc t										tg at	е	293
			Gly														341
aag Lys	gat Asp	caa Gln	ttc Phe 30	ccc	gag Glu	gtg Val	tat Tyr	gtg Val 35	CCC	aca Thr	gtg Val	ttc Phe	gaa Glu 40	aac	tac Tyr		389
			atc Ile														437
gat Asp	acg Thr 60	gcc Ala	ggt Gly	cag Gln	gag Glu	gac Asp 65	tac Tyr	gat Asp	cga Arg	ctc Leu	cga Arg 70	CCC	ctg Leu	tcc Ser	tat Tyr	•	485
	gat		gat Asp														533
tcg			aac Asn							ccc					ttc		581
			gtg Val 110						gga					ttg			629
aat Asn	gat Asp	CCC Pro 125	aat Asn	acc Thr	atc Ile	aag Lys	gag Glu 130	ttg Leu	ggc Gly	aag Lys	atg Met	aaa Lys 135	caa	gaa Glu	ccg Pro	•	677
			gaa Glu				aca									•	725
			gag Glu													. *	773
ttt Phe	gag Glu	aca Thr	gcc Ala	acc Thr 175	cga Arg	gcg Ala	gca Ala	tta Leu	cag Gln 180	gtc Val	aag Lys	aag Lys	aaa Lys	aag Lys 185	aag		821
			gtt Val 190			taat	gtc	gga a	acca	aaco	a t	ttt	ccta	t			869
tctt	atta	acc 1		tcat	c at	caac	atca	a aca	tcct	tca	acca	acaaa	ata (	caact	acaad	3 .	929
tatt	cacta	ata (	cttct	acta	ac ta	ıtgga	cgcg	g ato	ettaa	attt	agto	egcaa	att a	atcaa	ttggg	<b>3</b> - "	989
gaaa	attta	acg g	gaata	aaaa	a ga	accct	gaga	aca	aaaa	ıaaa	aaaa	ıaaaa	aa a	aaaa			104

<sup>&</sup>lt;210> 378 <211> 192 <212> PRT

<sup>&</sup>lt;213> Tigriopus japonicus

Met Ala Ala Ile Arg Lys Lys Leu Val Ile Val Gly Asp Gly Ala Cys	
Gly Lys Thr Cys Leu Leu Ile Val Phe Ser Lys Asp Gln Phe Pro Glu	
Val Tyr Val Pro Thr Val Phe Glu Asn Tyr Val Ala Asp Ile Glu Val	
Asp Gly Lys Gln Val Glu Leu Ala Leu Trp Asp Thr Ala Gly Gln Glu	
Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Asp Thr Asp Val Ile	
Leu Met Cys Phe Ser Ile Asp Ser Pro Asp Ser Leu Glu Asn Ile Pro 85 90 95	
Glu Lys Trp Thr Pro Glu Val Lys His Phe Cys Pro Asn Val Pro Ile 100 105 110	
Ile Leu Val Gly Asn Lys Lys Asp Leu Arg Asn Asp Pro Asn Thr Ile 115 120 125	
Lys Glu Leu Gly Lys Met Lys Gln Glu Pro Val Lys Pro Glu Glu Gly 130 135 140	
Arg Thr Met Ala Glu Lys Ile Asn Ala Phe Ala Tyr Leu Glu Cys Ser 145 150 155 160	
Ala Lys Ser Lys Glu Gly Val Arg Glu Val, Phe Glu Thr Ala Thr Arg 165 170 175	
Ala Ala Leu Gln Val Lys Lys Lys Lys Lys Pro Cys Val Leu Phe 180 185 190	
<210> 379 <211> 1014	
<212> DNA <213> Rhopalosiphum padi	
<220>	
<221> CDS <222> (197)(772)	
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tacactccgt acacaggttg gagatcgctg caggcagcgt tcgattgcga caacgacgac	120
cagcgagaac acttctctag tgctctgtgc tgcttattca ccagtgtaca cgtaggagtg	180
ttcccatage ggcaac atg cag ace atc aag tgc gtt gtt gtt ggt gat gga	180 232
ttcccatage ggcaac atg cag acc atc aag tgc gtt gtt gtt ggt gat gga Met Gln Thr Ile Lys Cys Val Val Gly Asp Gly 1 5 10	232
ttcccatagc ggcaac atg cag acc atc aag tgc gtt gtt gtt ggt gat gga  Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly  1 5 10  gct gtc ggt aag act tgt ctg ctc ata tcg tac aca aca aac aaa ttt Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Lys Phe	
ttcccatagc ggcaac atg cag acc atc aag tgc gtt gtt gtt ggt gat gga  Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly  1 5 10  gct gtc ggt aag act tgt ctg ctc ata tcg tac aca aca aac aaa ttt  Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Lys Phe  15 20 25  cct tca gaa tat gta ccg act gtt ttc gac aat tat gca gtg aca gtt	232
ttcccatagc ggcaac atg cag acc atc aag tgc gtt gtt gtt ggt ggt gga Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly  1 5 10  gct gtc ggt aag act tgt ctg ctc ata tcg tac aca aca aac aaa ttt Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Lys Phe  15 20 25  cct tca gaa tat gta ccg act gtt ttc gac aat tat gca gtg aca gtt Pro Ser Glu Tyr Val Pro Thr Val Phe Asp Asn Tyr Ala Val Thr Val  30 35 40	232 280
ttcccatagc ggcaac atg cag acc atc aag tgc gtt gtt gtt ggt gat gga  Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly  1 5 10  gct gtc ggt aag act tgt ctg ctc ata tcg tac aca aca aac aaa ttt Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Lys Phe  15 20 25  cct tca gaa tat gta ccg act gtt ttc gac aat tat gca gtg aca gtt Pro Ser Glu Tyr Val Pro Thr Val Phe Asp Asn Tyr Ala Val Thr Val  30 35 40  atg att ggt ggg gaa cca tac aca tta ggt tta ttt gat aca gca ggt Met Ile Gly Gly Glu Pro Tyr Thr Leu Gly Leu Phe Asp Thr Ala Gly	232 280 328
ttcccatagc ggcaac atg cag acc atc aag tgc gtt gtt gtt ggt gat gga  Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly  1 5 10  gct gtc ggt aag act tgt ctg ctc ata tcg tac aca aca aac aaa ttt Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Lys Phe  15 20 25  cct tca gaa tat gta ccg act gtt ttc gac aat tat gca gtg aca gtt Pro Ser Glu Tyr Val Pro Thr Val Phe Asp Asn Tyr Ala Val Thr Val  30 35 40  atg att ggt ggg gaa cca tac aca tta ggt tta ttt gat aca gca ggt Met Ile Gly Gly Glu Pro Tyr Thr Leu Gly Leu Phe Asp Thr Ala Gly 45 50 55 60  cag gaa gat tat gat cgc ctc aga cct ttg agt tat cca caa act gat	232 280 328
ttcccatagc ggcaac atg cag acc atc aag tgc gtt gtt gtt ggt gat gga  Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly  1 5 10  gct gtc ggt aag act tgt ctg ctc ata tcg tac aca aca aca aca aca ttt Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Lys Phe  15 20 25  cct tca gaa tat gta ccg act gtt ttc gac aat tat gca gtg aca gtt Pro Ser Glu Tyr Val Pro Thr Val Phe Asp Asn Tyr Ala Val Thr Val  30 35 40  atg att ggt ggg gaa cca tac aca tta ggt tta ttt gat aca gca ggt Met Ile Gly Gly Glu Pro Tyr Thr Leu Gly Leu Phe Asp Thr Ala Gly  45 50 55 60  cag gaa gat tat gat cgc ctc aga cct ttg agt tat cca caa act gat Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp  65 70 75	232 280 328 376 424
ttcccatagc ggcaac atg cag acc atc aag tgc gtt gtt gtt ggt gat gga  Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly  1 5 10  gct gtc ggt aag act tgt ctg ctc ata tcg tac aca aca aac aaa ttt Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Lys Phe  15 20 25  cct tca gaa tat gta ccg act gtt ttc gac aat tat gca gtg aca gtt Pro Ser Glu Tyr Val Pro Thr Val Phe Asp Asn Tyr Ala Val Thr Val  30 35 40  atg att ggt ggg gaa cca tac aca tta ggt tta ttt gat aca gca ggt Met Ile Gly Gly Glu Pro Tyr Thr Leu Gly Leu Phe Asp Thr Ala Gly 45 50 55 60  cag gaa gat tat gat cgc ctc aga cct ttg agt tat cca caa act gat Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp  65 70 75  gtg ttt ctt gtt tgt ttc tct gtg gtt tta cca tct tca ttt gaa aat Val Phe Leu Val Cys Phe Ser Val Val Leu Pro Ser Ser Phe Glu Asn	232 280 328 376
ttcccatage ggcaac atg cag acc atc aag tge gtt gtt ggt ggt gga gga Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly  1 5 10  gct gtc ggt aag act tgt ctg ctc ata tcg tac aca aca aaa attt Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Lys Phe  15 20 25  cct tca gaa tat gta ccg act gtt ttc gac aat tat gca gtg aca gtt Pro Ser Glu Tyr Val Pro Thr Val Phe Asp Asn Tyr Ala Val Thr Val  30 35 40  atg att ggt ggg gaa cca tac aca tta ggt tta ttt gat aca gca ggt  Met Ile Gly Gly Glu Pro Tyr Thr Leu Gly Leu Phe Asp Thr Ala Gly  45 50 55 60  cag gaa gat tat gat cgc ctc aga cct ttg agt tat cca caa act gat  Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp  65 75  gtg ttt ctt gtt tgt ttc tct gtg gtt tta cca tct tca ttt gaa aat  Val Phe Leu Val Cys Phe Ser Val Val Leu Pro Ser Ser Phe Glu Asn  80 85 90  gtc aaa gaa aaa tgg gtt ccg gag ata acg cat cac tgt caa aaa aca	232 280 328 376 424
ttcccatagc ggcaac atg cag acc atc aag tgc gtt gtt gtt ggt ggt gga Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly  1	232 280 328 376 424 472 520
ttcccatagc ggcaac atg cag acc atc aag tgc gtt gtt gtt ggt ggt gga  Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly  1 5 10  gct gtc ggt aag act tgt ctg ctc ata tcg tac aca aca aca aaa ttt Ala Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Lys Phe  15 20 25  cct tca gaa tat gta ccg act gtt ttc gac aat tat gca gtg aca gtt Pro Ser Glu Tyr Val Pro Thr Val Phe Asp Asn Tyr Ala Val Thr Val  30 35  atg att ggt ggg gaa cca tac aca tta ggt tta ttt gat aca gca ggt Met Ile Gly Gly Glu Pro Tyr Thr Leu Gly Leu Phe Asp Thr Ala Gly 45 50 55  cag gaa gat tat gat cgc ctc aga cct ttg agt tat cca caa act gat Gln Glu Asp Tyr Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp  65 70 75  gtg ttt ctt gtt tgt ttc tct gtg gtt tta cca tct tca ttt gaa aat Val Phe Leu Val Cys Phe Ser Val Val Leu Pro Ser Ser Phe Glu Asn  80 85 90  gtc aaa gaa aaa tgg gtt ccg gag ata acg cat cac tgt caa aaa aca Val Lys Glu Lys Trp Val Pro Glu Ile Thr His His Cys Gln Lys Thr	232 280 328 376 424 472

Thr 125	Val	Glu	Lys	Leu	Ala 130	Lys	aat Asn	Lys	.Gln	Lys 135	Ser	Ile	Ser	Phe	Glu 140	616
Gln	Gly	Glu	Lys	Leu 145	Ala	ГÀЗ	gaa Glu	Leu	Lys 150	Ala	Val	Lys	Tyr	Val 155	Glu	664
tgc Cys	tca Ser	gca Ala	ctt Leu 160	aca Thr	caa Gln	aaa Lys	gga Gly	cta Leu 165	aaa Lys	aat Asn	gta Val	ttt Phe	gat Asp 170	gaa Glu	gct Ala	712
att Ile	ctt Leu	gca Ala 175	gct Ala	tta Leu	gag Glu	cct Pro	cct Pro 180	gaa Glu	cca Pro	gtt Val	aag Lys	aag Lys 185	agg Arg	aag Lys	tgt Cys	760
gtt Val	ata Ile 190	ttg Leu	taag	getg	rcg g	rataa	ataa	la ca	ggtg	gegad	aat	tate	,tca	taaa	aatatt	819
taag	ataa	aa c	aatt	taaa	t ca	tgat	ttag	cat	ggat	aca	ataa	tgaa	at a	ataa -	ttatt	879 
ttgt	tttt	ac t	aato	tata	a at	atat	atat	ata	aata	att	tatt	ttat	at t	ttac	aagaa	939
aata	tgtg.	ca t	tcat	tgaa	t aa	taaa.	taaa	. tag	gttt	ttt	atac	gcca	aa a	aaaa	aaaaa	999
aaaa	aaaa	aa a	aaaa	L (												1014

<210> 380 <211> 191 <212> PRT

<213> Rhopalosiphum padi

<400> 380

Met Gln Thr Ile Lys Cys Val Val Val Gly Asp Gly Ala Val Gly Lys 10 Thr Cys Leu Leu Ile Ser Tyr Thr Thr Asn Lys Phe Pro Ser Glu Tyr 20 Val Pro Thr Val Phe Asp Asn Tyr Ala Val Thr Val Met Ile Gly Gly 40 Glu Pro Tyr Thr Leu Gly Leu Phe Asp Thr Ala Gly Gln Glu Asp Tyr 55 60 Asp Arg Leu Arg Pro Leu Ser Tyr Pro Gln Thr Asp Val Phe Leu Val 70 75 Cys Phe Ser Val Val Leu Pro Ser Ser Phe Glu Asn Val Lys Glu Lys Trp Val Pro Glu Ile Thr His His Cys Gln Lys Thr Pro Phe Leu Leu 100 105 110 Val Gly Thr Gln Ile Asp Leu Arg Glu Asp Ala Thr Thr Val Glu Lys 115 120 125 Leu Ala Lys Asn Lys Gln Lys Ser Ile Ser Phe Glu Gln Gly Glu Lys 135 140 Leu Ala Lys Glu Leu Lys Ala Val Lys Tyr Val Glu Cys Ser Ala Leu 150 155 Thr Gln Lys Gly Leu Lys Asn Val Phe Asp Glu Ala Ile Leu Ala Ala 165 170 Leu Glu Pro Pro Glu Pro Val Lys Lys Arg Lys Cys Val Ile Leu 180 185

<210> 381

<211> 679

<212> DNA

<213> Hordeum vulgare var

<220>

<221> CDS

<222> (14)..(655)

<400> 381					
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Thr Val Gl	y Asp Gly	Ala Val Gly 20	Lys Thr Cys	atg ctc atc .Met Leu Ile 25	Cys Tyr
acc agc aa Thr Ser As	c aag ttc n Lys Phe	ccc acc gac Pro Thr Asp 35	tac ata ccc Tyr Ile Pro	acg gtg ttc Thr Val Phe 40	gac aat 145 Asp Asn
ttc agc gc Phe Ser Al 45	g aac gtg a Asn Val	gtg gcg gac Val Ala Asp 50	ggc acc acg Gly Thr Thr 55	gtg aat ttg Val Asn Leu	ggc ctt 193 Gly Leu 60
tgg gac ac Trp Asp Th	c gcc ggg r Ala Gly 65	cag gag gat Gln Glu Asp	tac aac cgg Tyr Asn Arg 70	ctg agg cct Leu Arg Pro	cta agc 241 Leu Ser 75
tac cgc gg Tyr Arg Gl	je gee gaë y Ala Asp 80	gtt ttc gtg Val Phe Val	ctt gcc ttc Leu Ala Phe 85	tcc ctt gtg Ser Leu Val 90	agc cga 289 Ser Arg
gct agc ta Ala Ser Ty 95	r Glu Asn	atc atg aag Ile Met Lys 100	aag tgg ata Lys Trp Ile	ccg gag ctt Pro Glu Leu 105	cag cat 337 Gln His
tac gcg cc Tyr Ala Pr 110	c ggc gta c Gly Val	cct gtt gtg Pro Val Val 115	ctg gta ggc Leu Val Gly	aca aaa ctg Thr Lys Leu 120	gat ctt 385 Asp Leu
Arg Glu As	sp Lys His	Tyr Leu Leu 130	Asp His Pro 135		Pro Val . 140
Thr Thr Al	la Gln Gly 145	Glu Glu Leu	Arg Lys Gln 150	gtt ggt gct Val Gly Ala	Leu Tyr 155 :
Tyr Ile Gl	lu Cys Ser 160	Ser Lys Thr	Gln Gln Asn 165	gtc aaa gct Val Lys Ala 170	Val Phe
Asp Ala Al	la Ile Lys 75	Val Val Ile 180	Gln Pro Pro	act aaa caa Thr Lys Gln 185	Arg Glu
aag aag aa Lys Lys Ly 190	aa aag aaa ys Lys Lys	cag cgt cgg Gln Arg Arg 195	gga tgt tct Gly Cys Ser	atg atg aac Met Met Asn 200	ttc agc 625 Phe Ser
		tgc ttc aaa Cys Phe Lys 210		tga aagagaagg	gt 672
tccttgc					679

<210> 382

<211> 213

<212> PRT

<213> Hordeum vulgare var

 Ado > 382

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 Phe Pro Thr Asp Tyr Ile Pro Thr Val Phe Asp Asn Phe Ser Ala Asn 35

 Val Val Ala Asp Gly Thr Thr Val Asn Leu Gly Leu Trp Asp Thr Ala 50

 Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala 65

 Asp Val Phe Val Leu Ala Phe Ser Leu Val Ser Arg Ala Ser Tyr Glu 85

 Asn Ile Met Lys Lys Trp Ile Pro Glu Leu Gln His Tyr Ala Pro Gly

									201/2	<b>91</b> .									
				100					105					110					
			115				Gly	120					125			-			
		130					Pro 135					140							
	Gly 145	Glu	Glu	Leu	Arg	Lys 150	Gln	Val	Gly	Ala	Leu 155		Tyr	Ile	Glu	Cys 160			
	Ser	Ser	Lys	Thr	Gln 165		Asn	Val	Lys	Ala 170		Phe	Asp	Ala	Ala 175				
	rys	Val	Val	Ile 180	Gln	Pro	Pro	Thr	Lys 185	Gln	Arg	Glu	Lys	Lys 190		Lys			
			195		•		Ser	Met 200		Asn	Phe	Ser	Gly 205	Arg	Lys	Met			
	Leu	Cys 210	Phe	Lys	Ser										*				
	<21	0> 3	83			•											•		
	: -	1> 7		•		•	· · ·					٠.	- •		•		•		
		2> D			_										,		•		
	<21	3 > H	orde	um vi	ulga	re va	ar							• •					
	<22	0>							•										
		1> C	DS																
	<22	2> (	33).	. (689	9)														
	.40															•			
		0> 3		Tarrar	raa a	ar r:	agagg	72 <i>(</i> 72)	~ ~~	2+4	. 2		~~~	~~~	~~~	~~~			
	gga	cce	uug s	Jagas		ay y	agag	jaya	y ac	Met 1	Ser	Gly	Gly	Ala	Gly	Ala		5	3
	gcg	acg	gcg	gtg	agc	agg	ttc	atc	aag	tgc	gtg	gcc	gtg	ggc	gac	qqc		1	.01
	Ala	Thr	Ala 10	Val	Ser	Arg	Phe	Ile 15	Lys	Cys	Val	Ala	Val 20	Gly	Asp	ĞÎy			
	gcc	gtg	ggc	aag	acc	tgc	atg	ctc	atc	tgc	tac	acc	tgc	aac	aag	ttc	•	1	49
	Ala	Val 25	Gly	Lys	Thr	Cys	Met	Leu	Ile	Cys	Tyr	Thr	Cys	Asn	Lys	Phe			
	ccc		qac	tac	atc	ccc	acc	ata	ttc	gac	aac		agc	acc	aat	atc		1	97
	Pro 40	Thr	Asp	Tyr	Ile	Pro 45	Thr	Val	Phe	Asp	Asn 50	Phe	Ser	Ala	Asn	Val 55			
	tcc	gtg	gac	ggg	agc	atc	gtc	aac	ctc	ggc	ctc	tgg	gac	acc	gca	qqt		2	45
					60		Val			65				٠.	70				
	cag	gag	gat	tac	agc	agg	ctg	agg	cct	ctg	agc	tac	agg	gga	gcc	gat		2	93
				75			Leu		80					85		_			
	gtc	Dhe	atc	Ctc	tcc	Dhe	tcc Ser	ctc	acc	agc	aga	gca	agc	tat	gag	aat	•	3	41
	vaı	FIIC	90	шеu	per	FITE	Ser	95	1111	SEL.	Arg	ALG	100	TAT	GIU	ASII	•	٠.	
•	gtg	cac	aag	aag	tgg	atg	ccg	gag	ctt	cgc	cgg	tac	gcc	CCC	ggc	att		3	89
	Val		Lys	Lys	Trp	Met	Pro	Glu	Leu	Arg	Arg		Ala	Pro	Gly	Ile			
	cat	105 ota	cta	ctt.	att	aa.	110 acc	aacr	tta	cat	ata	115	as a	ά=+	202	aat		٠,	27
	Pro	Val	Leu	Leu	Val	Gly	Thr	Lvs	Leu	Asp	Leu	Ara	Glu	Asp	Arg	Ala		4	37
	120					125					130			_	_	135			
	tat	ctt	gct	gat	cat	gca	gct	gat	tcc	atc	ata	aca	act	gag	cag	ggt		4	85
	lyr	Leu	Ala	Asp	H1S 140	Ala	Āla	Asp	Ser	11e 145	Ile	Thr	Thr	Glu	Gln 150	Gly			
	gag	gat	ctt	agg		caa	ata	ggt	qct		qca.	tac	ata	gaa		agc		: 5	33
	Glu	Asp	Leu	Arg	Arg	Gln	Ile	ĞĬy	Ala	val	Āla	Tyr	Ile	Glu	Cys	Ser			
	taa	224	303	155	200	226	-+-		160					165				_	
	Ser	Lvs	Thr	Gln	Ara	Asn	att Ile	Lvs	Ala	Val	Phe	Asp	acc Thr	gca	TIA	aag		5	81
			170					175				_	180			-			
•	gcg	gtt	ctt	caa	cct	caa	agg:	cac	aag	gag	gta	gcc	aga	aaq	gaa	act		6	29
	Ala		Leu	Gln	Pro	Gln	Arg	His	Lys	Glu	Val		Arg	Lys	Glu	Thr			
	caa	185 aca	cac	tet	act	caa	190 tca	ata	a.c.c	cac	tac	195	tat	خص	a~+	+a+ ·		٠,	
	Arg	Thr	Arg	Ser	Ser	Arg	Ser	Val	Arg	Gln	Tyr	Phe	Cys	Glv	Ser	Ser		0	77
	200		_			205	-				210	_	• -	-2		215			

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	-								•						•		
agg Arg	ccg Pro	ctg Leu	agc Ser	tac Tyr 75	aga Arg	ggc	gcc Ala	gac Asp	gtg Val 80	ttc Phe	gtg Val	ctc Leu	gcc Ala	ttc Phe 85	tcc Ser	٠	295
ctc Leu	atc	agc Ser	agc Ser 90	gcc Ala	agc Ser	tac Tyr	gag Glu	aat Asn 95	gtt Val	ctt Leu	aag Lys	aag Lys	tgg Trp 100	atg Met	cca Pro		343
Glu	ctc Leu	Arg 105	Arg	Phe	Ala	Pro	Asn 110	Val	Pro	Ile	Val	Leu 115	Val	Gly	Thr		391
Lys	cta Leu 120	Asp	Leu	Arg	Asp	His 125	Arg	Ala	Tyr	Leu	Ala 130	Asp	His	Pro	Gly		439
Ala 135	tca Ser	Ala	Ile	Thr	Thr 140	Ala	Gln	Gly	Glu	Glu 145	Leu	Arg	Lys	Gln	Ile 150		487
Gly	gcc	Ala	Ala	Tyr 155	Ile	Glu	Cys	Ser	Ser	Lys	Thr	Gļn	Gln	Asn 165	Val		535
aag Lys	gct Ala	gtg Val	ttt Phe 170	gac Asp	acc Thr	gcc Ala	ata Ile	aag Lys 175	gtg <b>V</b> al	gtc Val	ctc Leu	cag Gln	ccg Pro 180	ccg Pro	agg Arg		583
aga Arg	agg Arg	gag Glu 185	gtg Val	atg Met	tcc Ser	gcc Ala	agg Arg 190	aag Lys	aaa Lys	acc Thr	agg Arg	cga Arg 195	agc Ser	tct Ser	gga Gly		631
tgc Cys	tcc Ser 200	atc Ile	aag Lys	cac His	ttg Leu	atc Ile 205	tgc Cys	GJÀ aaa	agt Ser	acg Thr	tgc Cys 210	gct Ala	gct Ala	tgaa	ittagca		683
cca	tggag	gc c	:tgga	ictga	c tá	tgga	gatg	aag	cate	19				•		1	721

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210

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<210> 388
<211> 197
<212> PRT
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<sup>&</sup>lt;213> Hordeum vulgare

				٠, ,					LUJIL	17,1								
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	Glu 65	Asp	Tyr	Ası	Arg	Leu .70		Pro	Lev	. Ser		Arg	Gly	Ala	a Asp	Val		
			. Leu	Ala	Phe 85		Leu	Ile	e Ser	Lys	75 Ala	Ser	Туг	Glu		80 Val		
	Thr	Lys	Lys	Trp	Ile	Pro	Glu	Lev		His	Туг	.Ala	Pro			. Pro		
	Ile	: Ile	Leu 115	. Val		Thr	Lys				Arg	Asp				Phe		
	Phe	Val	. Asp		Pro	Gly				Ile	Ser				Gly	Glu		
	Glu 145	Leu		Lys	Val	Ile 150			Thr	··Ala	Tyr 155			Cys	Ser	Ser	•	
			Gln	Gln	Asn 165	Ile		Ala	Val	Phe	Asp		Ala	Ile			٠	
	Val	Leu	Gln	Pro	Pro		Gln	Lys	Arg 185	Lys		Arg	Lys	Ser			•	
	Gly	Cys	Ser 195	Ile	Leu				,103					.130				
		0> 3				. •										٠.		
	<21	1> 6 2> D	NA															
			orde	um v	ulga	re			,			•						
		1> C				•												
			27).	. (66	8)						:							
		0> 3 tcct		cgtc	catt	ta g	ccgg									c atc e Ile		53
	аас	tac	atc	acc	gtc	aaa	gac	1				5			-			101
	Lys 10	Cys	Val	Thr	Val	Gly 15	Asp	Gly	Ala	Val	Gly 20	Lys	Thr	Cys	Met	Leu 25		
-	atc Ile	tgc Cys	tac Tyr	acc Thr	agc Ser 30	aac Asn	aag Lys	ttc Phe	ccc Pro	acc Thr 35	gac Asp	tac Tyr	gtg Val	ccc Pro	Thr	gtg		149
	ttc Phe	gac	aat	ttc	agc Ser	gcg	aac	gtg	gtg	gtg	gac	ggc	acc	acc	40 gtg	aac	•	197
				45	gac				50			_		55				245
	Leu	Gly	Leu 60	Trp	Asp	Thr	Ala	999 Gly 65	Gln	Glu	Asp	Tyr	Asn 70	Arg	Leu	Arg	•	245
	ccg Pro	ctg	agc	tac	cgg Arg	gga Gly	gcc Ala	gac	gtc Val	ttc Phe	gtg Val	ctc Leu	tcc	ttc Phe	tcg Ser	ctc Leu		293
		75·			agc		80			,		85						341
	Val 90	Ser	Arg	Āla	Ser	Tyr 95	Ğlü	Asn	Val	Met	Lys 100	Lys	Trp	Leu	Pro	Glu 105		J
	ctt Leu	cag Gln	cac His	cat His	gca Ala	ccc Pro	ggc Gly	gtg Val	cca Pro	aca Thr	gtg Val	ctg Leu	gtt Val	ggt Gly	aca Thr	aag	•	389
					110 gaa					115				_	120	-		437
	Leu	Asp	Leu	Arg 125	Ğlu	Āsp	Lys	Gln	Tyr 130	Leu	Leu	Asp	His	Pro	Gly	Val		
	gtg Val	cct Pro	gtt Val 140	act Thr	aca Thr	gct Ala	cag Gln	Gly	gag Glu	gaa Glu	ctc Leu	cgc Arg	Lys	cac His	atc Ile	ggt Gly		485
٠	gca	act	tgt	tat	gtc	gaa	tgc	145 agc	tca	aag	aca	cag	150 cag	aat	gtc	aaa		533
		155			Val		160			_		165				_		
	Ala	Val	Phe	Asp	gct Ala	Ala	Ile Ile	aag Lys	gta Val	grg Val	Ile	aaa Lys	cct Pro	cca Pro	aca Thr	Lys		581
	170 cág	agg	gaa	agg	agg	175 aag	aag	aaa	gca	cgg	180 caa	gga	tgt	gca	tca	185 ttg		629
												٠.						٠.
							•						•					

Gln Arg Glu Arg Arg Lys Lys Ala Arg Gln Gly Cys Ala Ser Leu 190 195 ggt acc ctg tca aga agg aag ctg gca tgc ttc aag tgatcagtcg 675 Gly Thr Leu Ser Arg Arg Lys Leu Ala Cys Phe Lys 677 ac <210> 390 <211> 213 <212> PRT <213> Hordeum vulgare <400> 390 Met Ala Ser Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp 10 Gly Ala Val Gly Lys Thr Cys Met Leu Ile Cys Tyr Thr Ser Asn Lys Phe Pro Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn 40 Val Val Val Asp Gly Thr Thr Val Asn Leu Gly Leu Trp Asp Thr Ala 50 55 60 Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala 70 75 Asp Val Phe Val Leu Ser Phe Ser Leu Val Ser Arg Ala Ser Tyr Glu 90 95 Asn Val Met Lys Lys Trp Leu Pro Glu Leu Gln His His Ala Pro Gly 105 110 100 Val Pro Thr Val Leu Val Gly Thr Lys Leu Asp Leu Arg Glu Asp Lys 125 115 120 Gln Tyr Leu Leu Asp His Pro Gly Val Val Pro Val Thr Thr Ala Gln 130 135 140 Gly Glu Glu Leu Arg Lys His Ile Gly Ala Thr Cys Tyr Val Glu Cys 150 155 Ser Ser Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile 170 165 Lys Val Val Ile Lys Pro Pro Thr Lys Gln Arg Glu Arg Arg Lys Lys 190 1.85 180 Lys Ala Arg Gln Gly Cys Ala Ser Leu Gly Thr Leu Ser Arg Arg Lys 195 200 Leu Ala Cys Phe Lys 210 <210> 391 <211> 565 <212> DNA <213> Nicotiana tabacum <220> <221> CDS <222> (71)..(565) <400> 391 ctttttccaa tttcaactcc ataaaactaa gaagctagtg ttcttctttc ttatctttct 60 aattgatgag atg aat act agt agt agt gcc agt aat agt gct tct act 109 Met Asn Thr Ser Ser Ser Ala Ser Asn Ser Ala Ser Thr gca aca gga aca aag ttc atc aaa tgt gtg aca gtt gga gat ggt gct 157 Ala Thr Gly Thr Lys Phe Ile Lys Cys Val Thr Val Gly Asp Gly Ala 20 gtt ggc aag act tgc ctt ctc atc tcc tac act agc tgc ctt ctc atc 205 Val Gly Lys Thr Cys Leu Leu Ile Ser Tyr Thr Ser Cys Leu Leu Ile 40 tcc tac act age aac act ttt cca act gat tat gtg cca act gtt ttt 253

																•		
													•					
7	VO 20	05/01	4828												PC <sup>7</sup>	Γ/EP2	004/008	136
									287/2								•	
					50			·		55					60	Phe		
	gac Asp	aat Asn	ttc Phe	agt Ser	gct Ala	aat Asn	gtc Val	aat Asn	gtt Val	gat Asp	gly	aag Lys	att Ile	gtg Val	aat Asn	ttg Leu		301
	aat	ctt	t.gg	65 gat	act	act	aat	caa	70	. dat	tat	226	aaa	75 CEE	200	cct		349
	Gly	Leu	Trp 80	Asp	Thr	Ala	Gly	Gln 85	Glu	Asp	Tyr	Asn	Arg	Leu	Arg	Pro		343
	ctt Leu	agt Ser 95	tat Tyr	cga Arg	gga Gly	gct Ala	gac Asp 100	gtc Val	ttc Phe	ttg Leu	ctt Leu	gca Ala 105	Phe	tct Ser	ctc Leu	ata Ile		397
	agt Ser 110	agg Arg	cct Pro	agc Ser	ttt Phe	gaa Glu 115	aat Asn	ata Ile	tca Ser	aaa Lys	aag Lys 120	tgg Trp	gtt Val	cct Pro	gag Glu	cta Leu 125		445
	aga Arg	cat His	tat Tyr	gcc Ala	cca Pro 130	tca Ser	gtg Val	cct Pro	att Ile	gtt Val 135	ctt	gtg Val	gjà aaa	act Thr	aaa Lys 140	ttg Leu		493
	gat Asp	tta Leu	aga Arg	gag Glu 145	gac	aag Lys	cag Gln	ttt Phe	aga Arg 150	agg	gac Asp	tac Tyr	cct Pro	ggt Gly 155	gca	tct		541
	aca Thr	att Ile	tca Ser 160	aca Thr	gaa Glu	cag Gln	ggc Gly	tag					-		-			<b>565</b>
	-01/		20													• .	•	
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	<213	3 > N:	Lcot:	iana	taba	cum												
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				Ile 20	•		:		25					30 '	_	_		
	Thr	Cys	Leu 35	Leu	Ile	Ser	Tyr	Thr 40	Ser	Cys	Leu	Leu	Ile 45	Ser	Tyr	Thr		
		50		Phe			55					60						
	65			٧al		70					75			٠.		80		
		•		Gly	85					90		_			95	_		
	Arg	Gly	Ala	Asp 100	Val	Phe	Leu	Leu	Ala 105	Phe	Ser	Leu	Ile	Ser 110	Arg	Pro		
	COT	Dha	C12 11	7	TIO	C	T	T	M	77-7	D	<b>~7.</b>	<b>*</b> :	<b>-</b>	•			

Ser Phe Glu Asn Ile Ser Lys Lys Trp Val Pro Glu Leu Arg His Tyr 120 125 Ala Pro Ser Val Pro Ile Val Leu Val Gly Thr Lys Leu Asp Leu Arg

135 140

Glu Asp Lys Gln Phe Arg Arg Asp Tyr Pro Gly Ala Ser Thr Ile Ser 145 150 155 160

Thr Glu Gln Gly

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<211> 1057
<212> DNA
<213> Nicotiana tabacum
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120

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aattttggta tgcaatttta cgtactttct tgaggtattt ttttttttat gttca atg 178 Met gcc tca agt gct tca aga ttc atc aaa tgt gtc acg gtt ggt gat ggt 226 Ala Ser Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp Gly 15 10 274 gee gtt gga aag act tgt atg ett att tge tat ace agt aac aag tte Ala Val Gly Lys Thr Cys Met Leu Ile Cys Tyr Thr Ser Asn Lys Phe 25 20 ccc act gat tat gtt ccc aca gtg ttt gac aac ttc agt gcc aat gtg Pro Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn Val 322 40 35 370 gtt gtc gaa ggg acc aca gta aat tta ggt ctt tgg gat act gca ggc Val Val Glu Gly Thr Thr Val Asn Leu Gly Leu Trp Asp Thr Ala Gly **.6**5 55 caa gaa gat tat aac aga tta agg cca ctg agc tac cga gga gca gat 418 Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala Asp gtt ttt gtc cta gcg ttc tcc ttg gtt agt cgc gca agc tac gag aac Val Phe Val Leu Ala Phe Ser Leu Val Ser Arg Ala Ser Tyr Glu Asn 466 90 95 85 ata ctt aaa aag tgg att cct gaa ctt cag cat tat gct cct gga ata 514 Ile Leu Lys Lys Trp Ile Pro Glu Leu Gln His Tyr Ala Pro Gly Ile 105 100 ccg gtg gta tta gct ggc acc aaa ctt gat ctt cgt gag gat aag cac 562 Pro Val Val Leu Ala Gly Thr Lys Leu Asp Leu Arg Glu Asp Lys His 125 115 120 ttc ttg gct gat cat cct gga tta gtt cct gtc acc acc gcg cag gga 610 Phe Leu Ala Asp His Pro Gly Leu Val Pro Val Thr Thr Ala Gln Gly 140 145 135 658 gag gag cta cgg aaa caa att ggt gct gcc tat tac atc gaa tgt agc Glu Glu Leu Arg Lys Gln Ile Gly Ala Ala Tyr Tyr Ile Glu Cys Ser 150 155 tet aaa aca caa cag aat gtg aaa get gte ttt gat get gea ate aag 706 Ser Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile Lys 170 754 Val Val Ile Lys Pro Pro Gln Lys Gln Lys Glu Lys Lys Lys Gln Arg 185 cga gga tgt ctc atg aat gtg atg tgc gga agg aag ctc gtt tgt ttg 802 Arg Gly Cys Leu Met Asn Val Met Cys Gly Arg Lys Leu Val Cys Leu 205 200

855

915

975

1035

Lys 210

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atatccatgg ctttagcgtg ctgcctataa aacttacatt tctatcagaa cttttgtgac

gagcataatg tatttgtttt tccataaccc aacttactgc tggacggcct tgatttgtct

gtaaaatacg ttacttgcta ggtttatatt tcaagtacat gtattaattc tattaaacca

acaaaaaaaa aaaaaaaaa aa 1057

<sup>&</sup>lt;210> 394 <211> 210

<sup>&</sup>lt;212> PRT

<sup>&</sup>lt;213> Nicotiana tabacum

<sup>&</sup>lt;400> 394

Met Ala Ser Ser Ala Ser Arg Phe Ile Lys Cys Val Thr Val Gly Asp

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289/291
 Gly Ala Val Gly Lys Thr Cys Met Leu Ile Cys Tyr Thr Ser Asn Lys
 Phe Pro Thr Asp Tyr Val Pro Thr Val Phe Asp Asn Phe Ser Ala Asn
 Val Val Val Glu Gly Thr Thr Val Asn Leu Gly Leu Trp Asp Thr Ala
                         55
Gly Gln Glu Asp Tyr Asn Arg Leu Arg Pro Leu Ser Tyr Arg Gly Ala
Asp Val Phe Val Leu Ala Phe Ser Leu Val Ser Arg Ala Ser Tyr Glu
Asn Ile Leu Lys Lys Trp Ile Pro Glu Leu Gln His Tyr Ala Pro Gly
                                 105
Ile Pro Val Val Leu Ala Gly Thr Lys Leu Asp Leu Arg Glu Asp Lys
                             120
His Phe Leu Ala Asp His Pro Gly Leu Val Pro Val Thr Thr Ala Gln
Gly Glu Glu Leu Arg Lys Gln Ile Gly Ala Ala Tyr Tyr Ile Glu Cys
                                         155
Ser Ser Lys Thr Gln Gln Asn Val Lys Ala Val Phe Asp Ala Ala Ile
                                     170
Lys Val Val Ile Lys Pro Pro Gln Lys Gln Lys Glu Lys Lys Lys Gln
                                 185
Arg Arg Gly Cys Leu Met Asn Val Met Cys Gly Arg Lys Leu Val Cys
Leu Lys
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                                                                       26
<210> 397
<211>
      20
<212> PRT
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<213> consensus

<220>

<221> MISC FEATURE

<222> (1)..(20)

Xaa in postion 2 is any amino acid, Xaa in postion 4 is Val, Thr, Ile or Leu, Xaa in position 5 is Val, Ile or Leu, Xaa in position 9 is Ala or Gly, Xaa in position 10 is any amino acid, Xaa in position 14 is Cys, Ser or Ala, Xaa in position 15 is Leu or Met, Xa a in position 16 is Leu or Met, Kaa in position 17 is any amino a cid, Xaa in position 18 is any amino acid, Xaa in position 19 is Tyr or Phe, Xaa in position 20 is Thr, Ser or Ala.

<400> 397

Lys Xaa Val Xaa Xaa Gly Asp Gly Xaa Xaa Gly Lys Thr Xaa Xaa Xaa 1 10 15

Xaa Xaa Xaa Xaa 20

<210> 398

<211> 13

<212> PRT

<213> consensus

<220>

<221> MISC\_FEATURE

<222> (1)..(13)

<223> Xaa in postion 1 is Phe or Tyr, Xaa in position 3 is any amino ac id, Xaa in position 4 is any amino acid, Xaa in position 6 is Val, Ile or Glu, Xaa in position 9 is Val or Ile, Xaa in position 11 is Asp or Glu, Xaa in position 12 is any amino acid, Xaa in position 13 is Tyr or Phe.

<400> 398

Xaa Pro Xaa Xaa Tyr Xaa Pro Thr Xaa Phe Xaa Xaa Xaa 1 5 10

<210> 399

<211> 22

<212> PRT

<213> consensus

<220>

<221> MISC\_FEATURE

<222> (1)..(22)

<223> Xaa in postion 1 is Val, Ile or Tyr, Xaa in position 2 is any amin o acid, Xaa in position 3 is Leu, Val or Ile, Xaa in position 4 is any amino acid, Xaa in position 5 is Leu, Ile or Met, Xaa in position 6 is Trp or Phe, Xaa in position 9 is Ala or Ser, Xaa in position 12 is Glu or Asp, Xaa in position 13 is Asp or Glu, Xaa in position 14 is Tyr or Phe, Xaa in position 15 is any amino acid, Xaa in position 16 is Arg, Lys or Asn, Xaa in position 17 is Leu, Ile or Val, Xaa in position 19 is Pro, Ser or Thr, Xaa in position 20 is Leu or Met, Xaa in position 21 is Ser, Ala or Phe.

<400> 399

Xaa Xaa Xaa Xaa Xaa Asp Thr Xaa Gly Gln Xaa Xaa Xaa Xaa Xaa 1 5 10 15

Xaa Arg Xaa Xaa Xaa Tyr

<210> 400

<211> 143

<212> PRT

<213> consensus

<220>

<221> MISC FEATURE

<222> (1)..(143)

<223> Xaa in all postions is any amino acid.

<400> 400

Lys Xaa Val Xaa Val Gly Asp Gly Ala Xaa Gly Lys Thr Cys Leu Leu 1 5 10 15

Pro Xaa Xaa Tyr Xaa Pro Thr Val Phe Xaa Asn Xaa Xaa Xaa Xaa Xaa 30 35 40

Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Leu Xaa Leu Trp Asp Thr 45 50 55

Ala Gly Gln Glu Asp Tyr Xaa Arg Leu Arg Pro Leu Ser Tyr Xaa Xaa 60 65 70 75

Xaa Xaa Xaa Asp Val Xaa Xaa Xaa Phe Ser Xaa Xaa Xaa Xaa Xaa IIO5

Xaa Ser Xaa Xaa Asn Xaa Xaa Xaa Lys Trp Xaa Pro Glu Xaa Xaa Xaa 110 115 120

Xaa Xaa Yaa Pro Xaa Xaa Pro Xaa Xaa Leu Val Gly Xaa Lys Xaa Asp 125 130 135

Leu Arg Xaa Asp

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

#### (54) Title: PROCESS FOR THE PRODUCTION OF FINE CHEMICALS IN PLANTS

(57) Abstract: The present invention relates to a process for the production of the fine chemical in a microorganism, a plant cell, a plant, a plant tissue or in one or more parts thereof. The invention furthermore relates to nucleic acid molecules, polypeptides, nucleic acid constructs, vectors, antisense molecules, antibodies, host cells, plant tissue, propagation material, harvested material, plants, microorganisms as well as agricultural compositions and their use.

pnal Application No PCT/EP2004/008136

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N15/82 C07K14/395 G01N33/50 C07K16/14 C12N5/10 A01H5/00 According to International Patent Classification (IPC) or to both national classification and IPC Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N C07K Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, Sequence Search, WPI Data, PAJ, BIOSIS, EMBASE, CHEM ABS Data C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Category 5 Citation of document, with Indication, where appropriate, of the relevant passages 1-26 "CHARACTERIZATION OF TWO MADAULE P ET AL: Χ MEMBERS OF THE RHO GENE FAMILY FROM THE YEAST SACCHAROMYCES CEREVISIAE" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 84, February 1987 (1987-02), pages 779-783, XP002038042 ISSN: 0027-8424 the whole document Patent family members are listed in annex. Further documents are listed in the continuation of box C. \*T\* later document published after the International filling date or priority date and not in conflict with the application but clied to understand the principle or theory underlying the invention Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filling date "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another cliation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family

Name and mailing address of the ISA

Date of the actual completion of the international search

28 January 2005

European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nf, Fax: (+31-70) 340-3016

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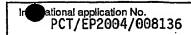
Burkhardt, P

Date of mailing of the International search report

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#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.2

Claims Nos.: 25 (partially)

Present claim 25 relates to a composition comprising a product defined by reference to a desirable characteristic or property, namely to act as an agonist or antagonist of the protein as defined by SEQ ID NO:2. The application does not provide support within the meaning of Article 6 PCT nor disclosure within the meaning of Article 5 PCT for such a product. In the present case, the claim so lacks support, and the application so lacks disclosure, that a meaningful search is impossible.

Independent of the above reasoning, the claim also lacks clarity (Article 6 PCT). An attempt is made to define a product within a process by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search impossible. The search has therefore been limited to those parts of the claim that appear to disclosed and supported, namely those parts relating to all other products comprised in the composition of claim 25 except the agonists and antagonists.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

Invention 1: Claims 1-26 (all partially)

relating to an isolated nucleic acid sequence (SEQ ID NO:1), the corresponding amino acid sequence (SEQ ID NO:2) and methods and products comprising said sequences.

Inventions 2-193: Claims 1-26 (all partially)

as invention 1 but relating to the isolated nucleic acid sequences with SEQ ID NOs:3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155, 157, 159, 161, 163, 165, 167, 169, 171, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231, 233, 235, 237, 239, 241, 243, 245, 247, 249, 251, 253, 255, 257, 259, 261, 263, 265, 267, 269, 271, 273, 275, 277, 279, 281, 283, 285, 287, 289, 291, 293, 295, 297, 299, 301, 303, 305, 307, 309, 311, 313, 315, 317, 319, 321, 323, 325, 327, 329, 331, 333, 335, 337, 339, 341, 343, 345, 347, 349, 351, 353, 355, 357, 359, 361, 363, 365, 367, 369, 371, 373, 375, 377, 379, 381, 383, 385, 387, 389, 391, 393 and the corresponding amino acid sequences with SEQ ID Nos:4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154, 156, 158, 160, 162, 164, 166, 168, 170, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230, 232, 234, 236, 238, 240, 242, 244, 246, 248, 250, 252, 254, 256, 258, 260, 262, 264, 266, 268, 270, 272, 274, 276, 278, 280, 282, 284, 286, 288, 290, 292, 294, 296, 298, 300, 302, 304, 306, 308, 310, 312, 314, 316, 318, 220, 222, 324, 326, 328, 330, 332, 334, 336, 338, 340, 342, 344, 346, 348, 350, 352, 354, 356, 358, 360, 362, 364, 366, 368, 370, 372, 374, 376, 378, 380, 382, 384, 386, 388, 390, 392, 394.

Inventions 194: Claims 1-26 (all partially)

relating to an amino acid sequence comprising the sequence motif as displayed in SEQ ID NO:47, nucleic acid sequence encoding said amino acid and methods and products comprising said sequences.

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Inventions 195-203: Claims 1-26 (all partially)

as invention 1 but relating to amino acid sequences comprising the sequence motifs as displayed in SEQ ID NOs:48, 49, 50, 51, 52, 397, 398, 399, 400.

Invention 204: Claims 2-26 (all partially)

relating to nucleic acid molecules apmplified from a library using the primers in SEQ ID NO:53 and methods and products comprising said sequence.

Invention 205: Claims 2-26 (all partially)

relating to nucleic acid molecules apmplified from a library using the primers in SEQ ID NO:54 and methods and products comprising said sequence.

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